Neurophysiological Processing of Architectural Ranking

Human Electrical Brain Responses to High- and Low-Ranking Buildings

Dissertation

zur

Erlangung der naturwissenschaftlichen Doktorwürde
(Dr. sc. nat.)

vorgelegt der

Mathematisch-naturwissenschaftlichen Fakultät

der

Universität Zürich

von

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Zürich, 2011

dedicated to

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ACKNOWLEDGEMENTS

This doctoral thesis was carried out at the departments of Neurophysiology and Neuropsychology at the Swiss Epilepsy Centre in Zurich under the guidance of Prof. Dr. Dr. med Thomas Grunwald, head of department of Clinical Neurophysiology.

I would like to express my sincere gratitude to the following:

- Prof. Dr. Dr. med Thomas Grunwald for sharing his immense experience and knowledge in all epilepsy and memory related questions, for his inspiration and support throughout my work, for his patience and critical reviews, and for tasteful musical discoveries.

- Prof. Dr. Hennric Jokeit for providing a colossal research office, for letting me be part of his team, and for tolerating my whistling.

- Prof Dr. Manila Vannucci for inspiring comments and relentless discussions, and for inspiring jealousy with her holiday reports.

- Prof. Dr. Lutz Jäncke and Prof. Dr. Stephan Neuhauss for supporting me again and submitting my PhD thesis to the faculty of science.

In addition, I am particularly indebted to:

- The wizards of EEG, Dr. Peter Hilficker, MSc. Ian Mothersill, and Dr. Nico Pezer for tireless and competent EEG support, for detecting the trickiest technical problems and for making artifacts disappear with a mere look.

- Mauri, Manu and Michel of the M-Team for repairing bits and bites and broken electrodes, and for being competitive darts players.

- Victoria Reed for correcting this thesis into proper English.

- Ninety-seven patients and healthy subjects for giving their time to participate in my studies.

Finally, I would like to give a special thanks to:

- My research colleagues for sharing both successes and drawbacks with me, for creative juggling breaks and refreshing swim outings.

- The NPSY team for pleasant coffee talks, tasty desserts and psychotherapy in the hallway.

- My family and friends for being patient, encouraging, and loyal throughout this time.

- My one and only, who always believed in me and who more than anyone deserved to see this work completed.

CONTENTS

ABBREVIATIONS

AED	Antiepileptic drug
EEG	Electroencephalogram
ERP	Event-related potential
fMRI	Functional magnetic resonance imaging
HS	Hippocampal sclerosis
MTL	Medial temporal lobe
TLE	Temporal lobe epilepsy
SAHE	Selective amygdala-hippocampectomy

ZUSAMMENFASSUNG

Gemäss einer aus der antiken Rhetorik stammenden und noch heute in der Architektur angewandten Theorie werden Gebäude gemäss dem Prinzip des Dekorums (lateinisch für "das, was sich ziemt") zwischen den Polen des profanen (niederen, oder "low-ranking") und dem sublimen (erhabenen, oder "high-ranking") kategorisiert. Während Ornamente mit high-ranking Charakter hauptsächlich für religiöse oder militärische Einrichtungen verwendet werden (z.B. Schlösser, Kirchen, oder Burgen), sind profane Häuser (z.B. Bauern- oder Wohnhäuser) häufig mit low-ranking Attributen ausgestattet.

Die vorliegende Doktorarbeit hatte zum Ziel, elektrophysiologische Korrelate der visuellen Verarbeitung des Dekorums zu untersuchen. Dazu wurden mittels der Methode des EEG (Elektroenzephalogramm) ereigniskorrelierte Potentiale (EKP) von Versuchspersonen gemessen während ihnen gezeichnete Bilder von entweder high-ranking oder low-ranking Gebäuden auf einem Bildschirm präsentiert wurden.

Ein erstes Experiment wurde durchgeführt, um zu untersuchen ob die EKPs von high- und low-ranking Gebäuden sich überhaupt unterscheiden würden. Die Resultate dieser Pilotstudie bestätigten dies und zeigten klare Unterschiede in den hirnphysiologischen Antworten auf Bilder von high- und low-ranking Gebäuden: im Zeitfenster zwischen 300 und 600 ms nach Stimuluspräsentation waren die Amplituden der EKPs von high-ranking Bildern signifikant positiver als diejenigen von low-ranking Stimuli. Interessanterweise scheinen diese Unterschiede unabhängig von bewusstem Erkennen zu sein, da die Versuchspersonen vorgängig nicht über die zwei verschiedenen Kategorien informiert gewesen sind.

Gemäss der ursprünglichen Theorie des architektonischen Dekorums sollten die als erhaben geltenden high-ranking Ornamente leichter dem Gedächtnis zugänglich sein als low-ranking Module, damit dem Beobachter die repräsentativen und wichtigen Gebäude besser in Erinnerung bleiben. Eine Folgestudie untersuchte daher, in wieweit der Hippokampus an der unterschiedlichen Verarbeitung dieser zwei Gebäudekategorien beteiligt ist, da diese Hirnstruktur eine zentrale Rolle in der Prozessierung Gedächtnis-relevanter Aufgaben besitzt. Zu diesem Zweck wurden neben gesunden Probanden auch Patienten mit einer Temporallappenepilepsie (TLE) mit und ohne Hippokampussklerose (HS) gemessen. Ähnlich den Resultaten

aus der Pilotstudie konnte auch in diesem Experiment gezeigt werden, dass die elektrophysiologischen Hirnantworten aller drei Versuchsgruppen in einem frühen Zeitfenster (200 bis 400 ms nach Stimuluspräsentation) high- von low-ranking Gebäuden unterscheiden. Allerdings zeigte sich zusätzlich, dass in einem späteren Zeitfenster (400 bis 600 ms) diese Unterscheidung bei Gesunden und bei TLE Patienten ohne HS zwar noch vorhanden war, bei TLE Patienten mit einer HS aber gänzlich fehlte. Eine Folgerung daraus lässt vermuten, dass der menschliche Hippokampus tatsächlich einen bedeutenden Einfluss in der Verarbeitung von high- und low-ranking Stimuli innehat.

Ausgehend von diesen Erkenntnissen ging eine dritte Studie schliesslich der Frage nach, ob sich in einem sogenannten Wiedererkennungs-Experiment die höhere Gedächtnisrelevanz der high-ranking Stimuli zeigen würde. Dazu wurden gesunde Probanden aufgefordert, sich in einer ersten Einprägungsphase Bilder von Gebäuden zu merken und in einer anschliessenden Testphase jeweils zu entscheiden, ob ein nun präsentiertes Gebäude zuvor bereits einmal gezeigt wurde (also "alt" ist) oder ob es vorher nicht dabei war (und also "neu" ist). Obwohl die Auswertung der Daten noch nicht vollständig abgeschlossen ist, lassen die vorläufigen Resultate bereits darauf schliessen, dass beide Gebäudekategorien anfällig für Wiederholungseffekte sind: in der Testphase zeigen die EKPs der "alten" wiedererkannten Stimuli eine positivere Amplitude im N400 Zeitfenster als diejenigen der "neuen". Zudem zeigen jedoch nur Gebäude der high-ranking Kategorie auch erhöte Amplituden in einer späten positiven Komponente (LPC, late positive component). Dies deutet darauf hin, dass die Verarbeitung von high-ranking Gebäuden mit Kategorie-spezifischen Selektionsprozessen assoziiert ist, welche mit Gedächtnis-relevanten Prozessen korreliert. Ein dritter Befund aus dieser Studie schliesslich weist einen sogenannten Dm Effekt nur für high-, nicht aber für low-ranking Gebäude auf. Der Dm Effekt beschreibt einen elektrophysiologischen Marker während der Einprägungsphase, welcher in der Testphase wiedererkannte Stimuli von später nicht mehr wiedererkannten Bildern unterscheidet. Die Tatsache, dass nur high-ranking Gebäude einen solchen Wiedererkennungswert zeigen, lässt vermuten, dass deren Verarbeitung mit einem erleichterten Zugang zum semantischen Netzwerk einhergeht. Dies widerspiegelt sich auch in der Beobachtung, dass EKPs von high-ranking Gebäuden mehr den EKPs von (einfach zu benennenden) Alltagsobjekten ähneln als den EKPs von low-ranking Gebäuden.

Zusammenfassend lassen die drei Studien dieser Dissertation darauf schliessen, dass neurophysiologische Korrelate der Verarbeitung von Gebäuden Aspekte des architektonischen Dekorums relfektieren, und dass Gebäude mit high-ranking Ornamenten einen höheren Grad der Vertrautheit hervorrufen (zumindest für Personen welche in der westlichen Kultur aufgewachsen sind).

Allgemein zeigen die hier vorliegenden Daten, dass die Differenzierung von high- und low-ranking Bildern sowohl eine frühe visuelle Objektselektion sowie eine spätere Objektkategorisierung beinhalten, und dass der Hippokampus wesentlich an diesem zweiten Schritt der visuellen Objektverarbeitung beteiligt ist.

SUMMARY

Since the ancient world architecture generally distinguishes two categories of buildings with either high- or low-ranking design. According to the theory of decorum, buildings designed to be high-ranking have more impact on the minds of their beholders than low-ranking buildings. Although previous studies have searched for brain activations elicited by buildings as such, few have looked at brain regions or processes differentiating between different *kinds* of buildings. In the present thesis, we conducted three experimental studies to investigate the visual object processing of drawings of buildings with either high- or low-ranking architectural ornaments.

Our first pilot study was designed to investigate whether event-related potentials (ERPs) reliably differentiate between stimuli of high- and low-ranking buildings at all. Therefore, we recorded ERPs of healthy subjects in a visual object categorization paradigm (VOCAP) using pictures of fictitious buildings and every-day life objects that were designed for the purposes of this thesis. Findings confirmed our hypothesis showing that ERP responses between 300 and 600 ms after stimulus presentation recorded over both frontal lobes were significantly more positive in amplitude to high-ranking buildings. Notably, the obtained differences seemed to be independent of conscious reflection as our subjects were not aware of the two different building categories.

A subsequent experiment aimed to identify possible contributions of the hippocampus by comparing normal subjects with patients suffering from temporal lobe epilepsies (TLEs) with (HS+) or without a hippocampal sclerosis (HS–). Replicating our previous findings, visual object categorization paradigm with patients (VOCAPPA) revealed early negative brain potentials between 200 and 400 ms that differentiated clearly between high- and low-ranking buildings in healthy subjects and TLE-patients both with and without HS. Moreover, results from this second study confirmed our hypotheses that the human hippocampus is, indeed, sensitive to the architectural decorum because, in contrast to the early time window, late positive potentials between 400 and 600 ms were higher in amplitude in response to high-ranking buildings only in healthy subjects and TLE patients without, but not in TLE patients with, HS. Thus, we were able to show for the first time that the human hippocampus proper does indeed contribute critically to architectural ranking inference and that this process is compromised in medial TLE with HS.

Since the hypothesized differential effects of high- and low-ranking stimuli may tap memory processes, we designed a visual recognition task as a third experiment (study and test of buildings, STEBS) to study possible memory processing of high- and low-ranking buildings during encoding and recognition. Although analysis of data is still ongoing / still in process, preliminary results of the STEBS study, in addition to replicating our prior findings, indicate that high- and low-ranking buildings show different ERP patterns during encoding and recognition-related memory processes: while both building categories seem to be sensitive to recognition effects, reflected in more positive amplitudes for old items during an early (N400) and a late (LPC) time window, increased LPC potentials for high-ranking buildings suggest that these pictures tap category selective processing already during the encoding phase. Lastly, a difference due to memory (Dm) effect was found only for high- but not for low-ranking buildings, indicating facilitated access to the semantic network associated with the encoding of high-ranking buildings.

In conclusion, we take our data to suggest that neurophysiological correlates of building perception reflect aspects of the architectural decorum, and that, following the desired effect of the decorum theory, high-ranking architectural designs are more familiar (at least to subjects raised in Western culture). More generally, our findings suggest that the differentiation between high- and low-ranking buildings entails both early visual object selection and late post-model selection processes and that the hippocampus proper contributes critically to this second stage of visual object categorization.

1 INTRODUCTION

One of the greatest challenges in neuroscience research today is to elucidate the structural, cellular and molecular basis of memory processes in humans. A crucial structure that is involved in memory formation is the hippocampus, a formation situated bilaterally within the medial temporal lobe (see Figure 1). Neurobiological research investigating the function of the hippocampal formation has allowed fundamental insights into how memory formation is organized within the human brain. For example, patients suffering from temporal lobe epilepsy (TLE), with structural or functional abnormalities in medial-temporal areas including the hippocampus, usually show impairments of declarative memory functions. Memory deficits, however, have a significant impact on quality of life. Therefore, the question of to what extend medial-temporal lesions are associated with neuropsychological impairments is especially relevant to patients with TLE. In this clinical population, as well as in healthy subjects, many studies have been carried out that have helped to establish a well-defined concept of human memory organization. These studies have shown the hippocampus to be a core structure involved in both the encoding and retrieval of memories. One of the main open questions, however, is how and to what extent the human hippocampus also participates in visual or perceptual processing. To this aim, the present thesis investigates whether the human hippocampus contributes to visual object identification and whether this process is modulated by cultural information. In addition, by combining an elaborate neurophysiological technique together with architectural stimuli derived from an established rhetorical theory, the present work sheds light on how the arts and neuroscience can unite to generate predictions that can be tested using neuroscientific methods.

1.1 Outline

Following the introduction, the second chapter of the thesis provides a brief description of epilepsy with a particular focus on temporal lobe epilepsy (TLE) and the characteristic clinical semiology of focal seizures originating within the medial temporal lobe. The third chapter presents an overview of how human memory is organized in the brain and to what extend the two hippocampal structures are involved. Research in human memory has traditionally drawn upon neuropsychological studies and findings from experiments with patients suffering

from circumscribed brain lesions. The fourth chapter, therefore, describes neurocognitive impairments that are typically found in TLE patients with hippocampal damage. Further, this chapter discusses the hippocampal contribution to visual and semantic processing, which marks a key question that triggered the experiments presented in this work. The present thesis examined the visual processing of newly designed architectural stimuli that are derived from a theory originating form rhetoric and design. Therefore, the last chapter of the introduction introduces the theory of the decorum and explains the concept of high- and low-ranking architecture, whose understanding remains essential throughout this thesis.

The sixth chapter provides a short introduction into the neurophysiological method of EEG and ERP recordings that was applied in the experiments. Following a discussion of the aims of the thesis, their general questions and hypotheses, three empirical studies will be presented in the form of independent manuscripts, two of which have been published in peer-reviewed journals. Due to ongoing analysis, however, only preliminary results of the third study are presented and the manuscript is presented as a draft version only. Following the manuscripts is a discussion of the main results of the empirical studies. Finally, the thesis closes with concluding remarks and an outlook for possible future work.

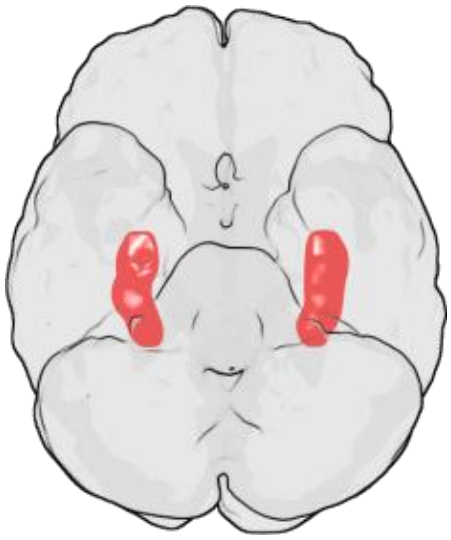

Figure 1. Location of the Hippocampus in the human brain. The figure shows the ventral view of a semi-transparent computer generated human brain with the red blobs indicating the approximate location of the two hippocampi inside the temporal lobes

1.2 Epilepsy

Apart from stroke, epilepsy is the second most common neurological disease (Duncan et al., 1995). Epileptic seizures are caused by excessive and hypersynchronous discharge of neuronal populations, which are hypothesized to be a consequence of a disequilibrium in the excitatory and inhibitory postsynaptic potentials. In general, interictal (between seizures) EEG may provide valuable information in lateralising the seizure focus in patients. For example, the interictal EEG signature of an epileptogenic focus in the medial temporal lobe (MTL) are unilateral or bilaterally independent mesial temporal spike and spike-and-wave complexes. If this discharge produces either subjective symptoms or objective signs it is regarded as a clinical seizure. By contrast, trains of epileptiform discharges in the electroencephalogram (EEG) in absence of any clinical signs are thought to represent subclinical seizure patterns. Clinical seizures are usually classified according to the International Classification of Epileptic Seizures (1981) and the diagnosis is confirmed by the capture of a typical episode during an EEG or video-EEG with epileptiform activity in (intracortical recordings) or over (surface EEG) the suspected brain regions (Devinsky 2004; Kilpatrick et al 2003).

1.2.1 Temporal Lobe Epilepsy

Among the various types of epilepsy, temporal lobe epilepsy (TLE) accounts for up to one third of all forms of epilepsy and is the most common type found in adults (Engel et al., 1997). While in lateral TLE seizures begin from the outer neocortex, seizures in mesial TLE (MTLE) typically arise from the inner parts of the MTL, including the hippocampus, parahippocampal gyrus, and amygdaly (Mathern et al., 2002). They are associated with specific anatomic changes within the MTL including tissue shrinkage, cell loss, and reactive gliosis (Mathern et al., 2002). Afterwards neuronal cells are replaced by glial cells, eventually leading to atrophy and sclerosis of the mesial temporal areas (Kalviainen et al., 2002; Mathern et al., 2002); hippocampal sclerosis (HS) eventually acts as predominant originator for TLE seizures in the medial temporal lobe (MTL). Today it is hypothesized that MTL sclerosis is both the cause and effect of seizures (Thom 2009).

Neuroimaging of anatomic lesions such as MTL sclerosis, are best revealed by high resolution magnetic resonance imaging (MRI). With the use of MRI, HS can be diagnosed by a reduction of hippocampal volume due to neuronal cell loss indicating atrophy and an increase of signal intensity indicating sclerosis (see Figure 2).

Mesial temporal lobe epilepsy is treated by medications. However, while half of patients respond to maximally tolerated doses of a single AED (Kwan et al 2001), most patients with TLE are pharmacoresistant (Leppik, 1992; Blümcke et al., 2002), meaning they do not become seizure free with adequate entiepileptic drug therapy.

In this case, refractory seizures are treated by resective surgery: After operative removal of the epileptogenic tissue, either through a selective amygdala-hippocampectomy (SAHE) or through a partial resection of the temporal lobe, 80 % of patients are expected to be seizure-free postoperatively (e.g. Zentner et al., 1995). The majority of TLE patients tend to show memory deficits that may vary in severity from mild subjective memory impairment to persistent amnesia that largely prevents the patient from learning any new information (Hermann et al., 1997). Risk factors for TLE include febrile seizures, meningitis, encephalitis or head trauma (Jokeit et al., 2004), and there is often a latency period of 5–10 years between the insult and the onset of seizures (Berg et al., 2003).

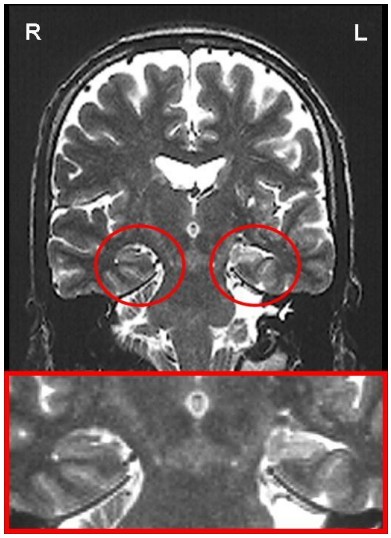

Figure 2. Magnetic resonance image and and enlargement of a hippocampus sclerosis. The sclerotic hippocampus on the left appears whiter and thinner compared to the intact contralateral structure.

1.2.2 Seizure semiology

TLE patients typically suffer from simple or complex partial seizures or–less frequently–from secondarily generalized tonic-clonic seizures, whose primary epileptogenic area includes the hippocampal formation. Postictal symptoms can help to lateralize the focus (i.e. impairment in verbal memory and naming after left-sided seizures and geographic disorientation after right-sided seizures). During simple partial seizures patients have preserved consciousness, and they typically

experience auras including epigastric sensations, emotional changes (mostly fear), and occasionally olfactory or gustatory hallucinations. Complex partial seizures, on the other hand, impair consciousness. They usually begin like simple partial temporal seizures but, in addition, include the symptoms of staring and arrest of motion, followed by altered responsiveness, oro-alimentary, and gestural automatisms (Devinsky 2004; Engel 1996).

1.3 Memory

For more than 5 decades, the medical records of one single patient have provided fundamental insights about how the human memory system is organized. In an attempt to halt his epileptic seizures, patient H.M. underwent a bilateral medial temporal lobe resection in the early 1950s which resulted in his inability to store new facts in long-term memory, while his immediate working memory remained more or less unaffected. Patient H.M.'s impairment in acquiring any new information, otherwise known as severe anterograde amnesia, was lifelong (Scoville and Milner, 1957; Corkin, 1984; Milner, 1968). H.M.'s neuropsychological performance was tested and studied excessively, yielding significant insights that eventually helped to establish definitions of distinct forms of human memory. For example, the fact that H.M. still had vivid memories from his early childhood, but could not remember anything new, indicates that the structures that store memories are separate from the mechanisms that encode them–at least in part, and that the hippocampus is likely to play a greater role in the latter.

1.3.1 Declarative and non-declarative memory

Functional and anatomical findings have shown that the two distinct memory systems differ with respect to explicit recall and “declarability" of memory items. Contents of the non-declarative memory system are implicit and can thus not be verbalized (Squire & Zola-Morgan 1991; Tulving & Markowitsch 1998). This memory system primarily entails conditioned reflexes like motor programs (e.g. riding a bicycle), and hence includes procedural memory. Declarative memory, on the other hand, contains explicit information that requires conscious awareness of the event to be encoded for memory followed by the transformation into an enduring memory trace (encoding) which enables the subsequent recollection of the event at a later time (retrieval). It is further divided into a semantic and an episodic part.

While semantic memory is associated with encyclopaedic or lexical knowledge that is acquired without additional contextual information (i.e. place or time the fact was learned), episodic memory refers to the cognitive process that enables the explicit, i.e. conscious, recollection of events and the context in which they occurred, eventually forming our individual autobiography.

Implicit memory is believed to be resistant against progressive or transient hippocampal damage because the associated information can be stored without participation of the hippocampus proper. By contrast, explicit encoding and recollection processes depend on the functional integrity of mesiotemporal structures including at least one hippocampus proper (Nadel et al., 2000). In this respect, patient H.M.'s performance reflected the specialization of the hippocampal formation: while performance of his non-declarative memory system was relatively preserved, damage to both hippocampi was correlated with impairments in his declarative, episodic memory, which also reflects the neuropsychological core deficit seen in the majority of patients with TLE (Eichenbaum 1999, McGaugh 2000).

1.3.2 Recollection and familiarity

Recognition of facts can be mediated either explicitly or implicitly: while "recollection" refers to the explicit memories including additional contextual information of the fact that was learned, implicit memories can elicit a subjective feeling of "familiarity" without explicit awareness of a previous encounter with a specific stimulus. Whether or not these two processes can be described by two qualitatively distinct mechanisms that are supported by different neural substrates is a major controversy in the current memory literature.

Authors in favor of the so-called "dual-process model" propose that familiarity and recollection are two different retrieval processes that independently contribute to recognition memory (for a review, see Yonelias, 2002). According to this theory, the entorhinal cortex contributes to familiarity-based recognition without additional contextual associative memory from the hippocampus. Data supporting this theory come from recent studies investigating patients and rats with restricted circumscribed hippocampal damage that revealed impaired recollection but spared familiarity performance (Eichenbaum et al., 2007; Vann et al., 2009; Aggleton et al., 2005). In addition, ERP studies have identified two topographically distinct ERP correlates (a parietal and a mid-frontal old/new component) that support the view that recognition memory can be divided into two dissociable and qualitatively distinct mechanisms

(Rugg and Curran, 2007). On the other hand, authors claiming that recognition is a continuous rather than a discrete memory process (Yovel and Paller, 2004; Voss and Paller, 2006; Paller et al., 2007) argue that both familiarity and recollection are continuously varying memory signals that are combined before a recognition judgment is made (Wixted, 2007). Supporting evidence comes from ERP studies revealing that neural correlates interpreted as familiarity effects more likely represent reflections of implicit rather than explicit memory processing (Paller et al., 2007; Voss and Paller, 2009). Furthermore, many experimental studies investigating recognition memory are not exclusively restricted to testing isolated familiarity modulations, but rather allow for parallel processing with conceptual priming (Rugg and Curran, 2007; Voss et al., 2008), thus offering only tentative interpretations.

1.4 Neuropsychology

Mesial temporal lobe epilepsy has become a major field of investigation in neuropsychological research, partly due to its relatively high prevalence. Not only the subject H.M. but also numerous other patients suffering from TLE have undergone extensive neuropsychological testing to elucidate the functional deficits that are associated with temporal lobe damage. The fact that the underlying structural lesion typically lies in a restricted and well circumscribed brain region allows one to draw conclusions on correlations between neurocognitive deficits and structural damage. The major finding of these studies is that mesial temporal structures, i.e. the hippocampus, parahippocampal area and amygdala, differentially contribute to memory processing in an essential way.

1.4.1 Neurocognitive impairments in TLE patients

Originally proposed by Milner & Kimura, the concept of material specific memory has remained influential over the last 40 years, triggering extensive research confirming its predictions (Milner 1958, 1968; Kimura 1963). According to this model, declarative memory impairments in TLE patients tend to be material specific as a function of the lateralization of the epileptic focus (Milner 1958). As a consequence, patients with a TLE originating from the left, usually dominant hemisphere tend to show deficits in the processing of verbal material (Helmstaedter et al., 1997; Jokeit et al., 2001; Moscovitch et al., 2002). Contrary, patients with damage in the right hemisphere are likely to show impairments in the processing of non-verbal, visual material

(perceptual details or spatial attributes) (Gleissner et al., 1998; Helmstaedter et al., 1991). Notably, while there is consensus that unilateral removal of temporal lobe structures in the left hemisphere is often associated with additional postoperative deficits in the verbal memory performance (Hermann et al., 1988; Helmstaedter and Elger, 1996), right-sided medial temporal resections usually do not increase preoperative existing visual memory deficits (Smith and Milner, 1981; Gleissner et al., 1998; Dietl et al. 2008). Conflicting evidence, however, come from studies showing that a right-sided selective amygdala-hippocampectomy does indeed lead to an impairment of the visual memory performance (e.g. Janszky et al., 2005). It is argued that the lack of visual deficits found in some cases may be explained by the fact that the experimental stimuli that were used to test visual memory in TLE patients may be suitable for verbalization (Helmstaedter et al., 1995). Thus, the intact contralateral (in this case dominant) hemisphere may compensate visual impairments by recruiting verbal mechanisms that are then applied to provide visual memory processing.

1.4.2 Hippocampal contribution to visual and verbal memory

In order to identify the epileptogenic focus, TLE patients undergo invasive presurgical evaluations with implanted medial temporal depth electrodes that are placed inside the medial temporal lobe (MTL). To increase the local resolution of the electrical activity recorded from local brain structures, intracortical depth electrodes may even pierce the hippocampal structure. Because patients remain conscious during the procedure, this experimental approach allows a parallel investigation of clinical electrophysiological and cognitive neuropsychological analyses, as they both are provided by the MTL structure. Consequently, much research has been done studying memory functions using intracranial ERP recordings.

For example, one major finding in verbal memory research is the identification of N400 potentials that are generated within the rhinal cortex in response to both words and pictures. This local field potential within the anterior MTL ("AMTL-N400") is associated with verbal novelty detection which is an important aspect supporting the encoding of verbal memory (Grunwald et al., 1999a; for a review see Grunwald, 2006). Importantly, the AMTL-N400 has been shown to be generated, at least in part, by the hippocampus proper because its amplitude to initial presentations ("new") but not to repetitions ("old") of words correlates selectively with the neuronal density within the hippocampal subfield CA1 (Grunwald et al., 1998).

Moreover, hippocampal novelty detection has been shown to be associated with successful encoding for declarative memory (Fernandez et al., 1999a, 1999b). Studies with patients suffering from TLE revealed that both the NMDA-receptor blocker ketamine and hippocampal sclerosis selectively reduce AMTL-N400 responses to words (Grunwald et al., 1998; Grunwald et al., 1999), thus suggesting a prominent role of the hippocampus proper in the formation of declarative memory.

In our own study we used a continuous recognition paradigm with words and nonwords to further investigate this novelty detection in healthy subjects and patients with TLE. We could show that, while ERPs of healthy subjects demonstrated a repetition effect both in the N400- and in a later P600 time-window for both words and nonwords, these effects were abolished in TLE patients, indicating that a dysfunctional hippocampus can compromise phonological or graphematical processing (Oppenheim et al., 2010c. *in prep.*). However, further analyses are necessary to study the specific impact of the side of epileptogenic lesion (i.e. left vs. right-sided TLE patients).

Likewise, there is supporting evidence suggesting that visual memory processes are also linked with the human hippocampus. For example, intracortical recordings show that only within intact but not in epileptic hippocampi ERPs could differentiate reliably between real and nonsense objects as well as between identified and unidentified visual objects (Vannucci et al., 2003, 2006). Moreover, hippocampal differentiation between real and nonsense objects was found only in patients with normal visual memory, but not in patients whose visual memory performance was reduced (Vannucci et al., 2008). In addition, a scalp potential called late positive complex (LPC or P600) that is related to hippocampal activity has been shown to be larger in amplitude to famous than to unfamiliar faces (Trautner et al., 2004; Dietl et al., 2005), and it is larger in response to words with high than to words with low imageability (Klaver et al., 2005). Thus, besides the formation of declarative memory, these data show that the human hippocampus is additionally involved in the semantic processing of visual stimuli to an extent that is crucially important for the formation of the visual memory.

To summarize, the two hippocampal structures contribute differentially to verbal and visual memory: while there is convincing evidence that the dominant left hemisphere provides verbal processes that can support not only verbal but also visual tasks, converging findings suggest that both the left and the right human hippocampus

proper contribute to the semantic or even perceptual (associative) processing for the identification of visual objects and verbalizable visual stimuli and that these contributions are directly linked to visual memory performance.

1.4.3 Hippocampal contribution to visual and semantic processing

Hippocampal damage seems to affect cognitive abilities beyond memory functions. In fact, echoing evidence from experiments with TLE patients suggesting that the MTL is involved in the processing of semantic information, functional brain imaging studies with healthy subjects have shown that MTL structures are not only involved in episodic memory formation but also in visual object processing: they are active during tasks requiring the processing of complex visual stimuli without any explicit learning and memory demands (Martin et al., 1997; Martin 1999; Vuilleumier et al., 2002), suggesting a contribution of MTL structures in the processing of different visual stimuli. In addition, imaging and neuropsychological studies with TLE patients has found object naming and verbal fluency to be influenced by hippocampal pathology (Rausch et al., 1993; Barr 1997; Lacritz et al., 2004). Intracortical recordings with TLE patients revealed a limbic response (the hippocampal-N300 potential) that was increased in response to unidentified compared to identified visual objects (Vannucci et al., 2006). Thus, these data suggest a specific role of the hippocampus proper in the retrieval of semantic and lexical information about visual objects stored in long-term memory or–more generally–in the semantic processing of visual stimuli (Vannucci et al., 2003, Vannucci 2007).

Nevertheless, these findings raise the questions of whether the same temporal lobe structures may subserve both visual perceptual and memory processes and whether deficits in visual processing in TLE patients may contribute to visual memory impairments. If the human hippocampus supports visual processing and if this participation is crucial for visual memory, it is tempting to hypothesize that the human hippocampus may be specifically activated by visual stimuli that were especially designed to convey significance and thus elicit memory processes. Therefore, we designed three visual object ERP experiments using pictures of buildings that were composed according to the architectural theory of the decorum.

1.5 The decorum

One theory in the arts that has remained influential for many decades and is being applied even in today's modern design is the concept of decorum. Originally emerging from rules of classical rhetoric, the decorum theory (Latin for "right, proper") proposes a system in which specific features designate the appropriateness of style. In this concept, specific words, movements, or actions are preserved for exclusive use to indicate a certain style of a poem, theatrical subject, or drama. Notably, the decorum theory is not restricted to one specific domain. Rather, its implication is widely observed in classical rhetoric, theatre, poetry, the Roman law, social science, and architecture. For example, many European inner cities are still characterized by Vignolian architecture which dates back to medieval times with state buildings and seats of government built using temple fronts and triumphal arches following the rule of the classical decorum system (Vignola-Barozzi, 1582). Even during the 20th and early 21st century the decorum theory has remained a central theme in architectural design. Thus, ranking of architectural ornaments and buildings follows–at least in Western cultures–rules of the architectural decorum.

1.5.1 High- and low-ranking architecture

Starting with Vitruv's fundamental work that outlined an architectural theory for the first time between 33 and 22 B.C. (Vitruvius, 1999) to Alberti's "Ten Books on Architecture", written in the middle of the 15th century (Alberti, 1485), and Vignola's most famous textbook of the Italian renaissance ("Rule of the Five Orders", Vignola-Barozzi 1582) architectural textbooks in Western culture have described how ornaments should be used to make buildings more prominent, attracting attention and eliciting a sublime feeling. For example, Alberti recognized in the arches, columns and temple formats the high-ranking attributes and ornaments which characterized "sublime" buildings designating higher ranking (Alberti, 1485). Accordingly, ornamental modules were classified according to the rules of the architectural decorum so that all buildings were designated higher or lower rankings ranging between the poles of the "sublime" and the "low" (Mühlmann, 1996). Those architectural modules and materials that served to signify higher rankings were designed to be outstanding while those associated with the low were not. In general, architectural stimuli indicating higher ranking were reserved for public sacral buildings and constructions associated with matters of military sovereignty while they were not used for buildings associated with economy or private life. By assigning

ornamental modules for the poles of high- and low-ranking buildings these ranking indications are accessible to semantic processing which in turn is provided by the human hippocampus.

2 AIMS AND GENERAL QUESTIONS OF THE THESIS

2.1 Aims of the thesis

The main questions of this thesis were whether and how the human hippocampus participates in the visual processing of objects. More specifically, the present work aimed at shedding light on neurophysiological mechanisms of the perception of high- and low-ranking buildings, stimuli that were designed according to the architectural decorum (see chapter 1.5). The experiments presented in this thesis measured brain electrical activity as indexed by event-related potentials (ERPs) to evaluate neurophysiological correlates of the visual processing of these stimuli.

Based on recent findings suggesting that the hippocampus is involved in the visual object processing and the formation of visual memory (Vannucci et al., 2003, 2006), a further purpose of our experiments was to investigate hippocampal contributions to the processing of architectural ranking by comparing healthy subjects and patients suffering from TLE with and without hippocampal sclerosis.

2.2 General questions

The theory of the decorum defines an architectural system of rules that adjusts the appropriateness of style and content to make specific buildings more ("high-ranking") or less prominent ("low-ranking") (see chapter 1.5). Although previous ERP studies have searched for brain activations elicited by buildings as such, few have looked at brain regions or processes differentiating between different *kinds* of buildings. Therefore, our first study was designed to investigate whether event-related potentials (ERPs) reliably differentiate between stimuli of high- and low-ranking buildings at all. In a next step, the second experiment aimed to identify possible contributions of the hippocampus by comparing normal subjects with patients suffering from temporal lobe epilepsies (TLEs) with (HS+) or without a hippocampal sclerosis (HS–). Since the hypothesized differential effects of high- and low-ranking stimuli may also tap memory processes, a visual recognition task was designed as a third experiment to study possible memory effects of high- and low-ranking buildings.

The following three questions summarize the main goals for the three studies that were performed:

General questions:

- *Do visual stimuli of buildings elicit electrical brain responses that differentiate between high- and low-ranking buildings?*
- *Is the processing of high- and low-ranking buildings affected by hippocampal damage?*
- *What role does the hippocampus proper play in the recognition of high- and low-ranking buildings?*

3 EXPERIMENTAL STUDIES

3.1 Summary of the studies

In this section brief summaries are first presented describing the three experiments that were conducted. This is followed by a description of the participants that were involved and the applied stimuli and designs we used. The present work comprises three experimental studies that are appended following this chapter. The first two studies (VOCAP and VOCAPPA) are presented in their original form as they have been published (see chapter 4). As the analysis of the results from the third study (STEBS) is still in process, only the abstract of this manuscript is attached and results will not be part of the general discussion.

3.1.1 The first study: Visual Object Categorization Paradigm

To examine differential electrical brain responses to high- and low-ranking buildings we designed a visual object categorization paradigm (VOCAP) using pictures of fictitious buildings with either high- or low-ranking architectural ornamental modules and pictures of every-day life objects (for a description of the stimuli, see chapter 3.3). If the desired effect of the decorum theory was true, high-ranking architectural designs should be more familiar (at least to subjects raised in Western culture). Many studies of brain electrical responses to visual and verbal stimuli have shown familiarity effects to be associated with a reduced N400-component, predominantly occurring over frontal electrodes (e.g. Mecklinger, 2006). Therefore, we hypothesized that:

Hypotheses of the first study:

- *Pictures of buildings with high and low-ranking attributes elicit specific electrophysiological potentials in a time-window approximately 400 ms after stimulus presentation.*

- *ERPs recorded in healthy subjects demonstrate a differentiation between high- and low-ranking buildings.*

The results of the first study confirmed that electrical brain responses of healthy subjects indeed differentiate between high- and low-ranking buildings. More specifically, ERPs between 300 and 600 ms after stimulus presentation recorded over both frontal lobes were significantly more positive in amplitude for high-ranking buildings compared to responses to low-ranking buildings. The obtained differences seemed to be independent of conscious reflection as our subjects were not aware of the two different building categories. Thus, we take our data to suggest that neurophysiological correlates of building perception reflect aspects of the architectural decorum. Since this rule system is ubiquitous in Western architecture, it may define architectural prototypes that may elicit familiarity memory processes.

3.1.2 The second study: Visual Object Categorization Paradigm with Patients

Based on the findings of our first experiment demonstrating ERP differences between high- and low-ranking buildings on the one hand, and the intended presumption of the architectural decorum, that high-ranking ornaments are thought to make buildings more prominent, thus familiar, on the other, our second study asked to what extend this distinction is mediated by the hippocampus and whether this process is affected by the presence of hippocampal damage.

Previous studies have shown that the human hippocampus is linked crucially with semantic processing of visual and visualizable verbal stimuli. Therefore, we recruited patients suffering from medial temporal lobe epilepsy (TLE) with and without hippocampal sclerosis (HS) in order to apply the same visual object categorization paradigm with patients (VOCAPPA) and examine the hippocampal contribution to the differentiation between high- and low-ranking buildings. Furthermore, by investigating patients with TLE with and without hippocampal damage we aimed to specifically explore the extent to which this process is supported by the human hippocampus. The hypotheses of our second study were as follows:

Hypotheses of the second study:

- *The hippocampus proper contributes crucially to the differentiation between high- and low-ranking buildings.*
- *The differentiation between high- and low-ranking buildings is impaired in TLE-patients with but not in TLE-patients without hippocampal sclerosis.*

In our second study, we were able to replicate our findings from the VOCAP study, revealing early negative brain potentials between 200 and 400 ms that differentiated clearly between high- and low-ranking buildings in healthy subjects and TLE-patients both with and without HS. Moreover, results from the VOCAPPA study confirmed our hypotheses that the human hippocampus is, indeed, sensitive to the architectural decorum because, in contrast to the early time window, late positive potentials between 400 and 600 ms were higher in amplitude in response to high-ranking buildings only in healthy subjects and TLE patients without, but not in TLE patients with, HS. Thus, we were able to show for the first time that the human hippocampus proper does indeed contribute critically to architectural ranking inference and that this process is compromised in medial TLE with HS. More generally, our findings suggest that the differentiation between high- and low-ranking buildings entails both early visual object selection and late post-model selection processes and that the hippocampus proper contributes critically to this second stage of visual object categorization.

3.1.3 The third study: Study and Test of Buildings

If the architectural decorum system should indeed have the desired differential effects on the minds and brains of the beholders of buildings, it should make high-ranking buildings more memorable. Therefore, our third experiment was designed to investigate the study and test of buildings (STEBS). In this visual recognition task subjects had to memorize and recognize pictures of high- and low-ranking buildings. We hypothesized that:

Hypotheses of the third study:

- *Recognition performance is better for high-ranking than for low-ranking buildings.*
- *There is a larger "difference to memory" effect for high-ranking than for low-ranking buildings.*

In addition to repclicating prior data by showing that high- and low-ranking stimuli can be reliably dissociated by ERP-responses, preliminary results of the STEBS experiment indicate that high- and low-ranking buildings show different ERP patterns during encoding and recognition-related memory processes: while both building categories seem to be sensitive to recognition effects, reflected in more positive

amplitudes for old items during an early (N400) and a late (LPC) time window, increased LPC potentials for high-ranking buildings suggest that these pictures tap category selective processing already during the encoding phase. Lastly, a *difference to memory* (Dm) effect was found only for high- but not for low-ranking buildings, indicating facilitated access to the semantic network associated with the encoding of high-ranking buildings.

3.2 Participants

Participants were recruited via announcements at the University of Zurich or from the Swiss Epilepsy Center in which all the studies were performed. No financial compensation was given and no subject participated in more than one study. Respecting the fact that the decorum theory has been developed in and applied to Western Culture, we excluded participants that were born and raised outside Central Europe. To further exclude any training effect that might interfere with visual evoked potentials, none of the subjects had previous qualification in visual arts or architecture, and none of them reported to be particularly interested in reading books or periodicals about these fields. As intact visual perception was necessary, we assured that all participants had normal or corrected-to-normal vision (i.e., wearing glasses or contact lenses). The experimental procedure was thorooughly explained to the subjects in both oral and written form and they were given the chance to ask questions if any unclarities remained. Throughout the measurements, the experimenter was present next to the participants in the same room. Finally, all participants gave informed and written consent and the study was approved by the local medical ethics committee and was in compliance with the Declaration of Helsinki.

3.2.1 Healthy subjects

In total, 45 healthy subjects participated in the three studies (13 in the VOCAP, 14 in the VOCAPPA, and 18 in the STEBS experiment). Twenty-six were females and three were left-handed. The age range was 21-64 with a mean age of 34 years. None had any skull defects or had undergone any neurosurgical procedures and all fulfilled the above mentioned inclusion criteria.

3.2.2 Patients

A total of 30 TLE patients volunteered to participate in the VOCAPPA study. They were recruited on the basis of their clinical records and their appointment schedule in the clinic. Whenever possible, ERP measurements of patients were conducted as in-patients while they were already fitted with EEG electrodes. In some cases, however, electrodes had to be placed especially for the purpose our experiment.

In all patients diagnosis of unilateral TLE with partial and/or secondary generalized tonic clonic seizures was based on typical clinical seizure semiology, interictal and ictal EEG findings and the results of MRI scans which demonstrated unilateral hippocampal sclerosis (HS) in 20 patients (10 with right- (RTLE), and 10 with left-sided temporal lobe epilepsy (LTLE)). Only patients with no additional (extrahippocampal) damage were included in this group. To compare the effect of TLE with and without hippocampal sclerosis, 10 more patients either with different lesions within the temporal lobe (e.g. parahippocampal, amygdala) not affecting the hippocampus or without any morphological abnormalities in their MRI scans were defined as the HS– group.

Twenty-five patients were right-handed and 15 were females. In all of the 5 patients that were left-handed functional magnetic resonance imaging indicated (typical) left-sided language dominance which allowed their data to be collapsed with those from right-handed patients with regards to functional specialization of the hemispheres. The age range was 18–57 with a mean age of 39.9 years. There was no difference between the groups of HS+ and HS– or between LTE and RTE patients with regard to mean age, duration of epilepsy or age at seizure onset (for an overview of patient's data, see Table 1).

3.3 Stimuli

Following the rules of the decorum system (see chapter 1.5) we designed pictures of fictitious buildings representing the two categories of "high-" and "low"-ranking. All stimuli were black-and-white drawings exclusively produced by a professional graphic artist for the purposes of this experiment, taking specific care of comparable size, contrast, and brightness (for examples of stimuli, see Figure 4). We classified our stimuli according to the composition and nature of decorated ornamental modules and arranged these modules according to their supposed ranking

postulated by the decorum system (from high to low: archway, Doric, Ionic, Corinthian columns and temple facades, upright format of facades, landscape format of facades, cottage) along both axes of a matrix. Randomly chosen intersections in this array thus determined the composition and nature of ornaments for a building. Along the diagonal of the matrix, buildings characterized by more high-ranking attributes were defined as "high-" and those with more low-ranking attributes as "low-ranking" architectural stimuli. In addition, pictures of normal everyday life objects were designed and served as second target ("objects") for the VOCAP and VOCAPPA, respectively.

Since we were interested in memory processes, special attention was paid to avoid resemblances of our stimuli with real existing buildings in order to prevent possible confounding variables with subjects' episodic memories. Therefore, all stimuli had been presented to several research colleagues first in order to exclude any items that were rated as being too similar to a building existing in reality.

3.4 Study designs

3.4.1 Method

The experimental procedure in all three studies was ERP recordings with data obtained from 23 electrodes (including one reference and one ground electrode, see Figure 3) placed on the scalp using either an elastic cap or, in the case of in-patients, electrodes that were manually placed on the scalp according to the international 10/20 system. Data were obtained using a DC amplifier with a sampling rate of 256 Hz per channel. They were offline re-referenced to linked mastoids and bandpass filtered with 0.03-30 Hz (12 dB/ oct). ERP components of 1200 ms duration including a 200 ms pre-stimulus baseline were selectively averaged and manually rejected if contaminated with artifacts. For statistical analyses, mean amplitudes of selected time windows were calculated using repeated measures analysis of variance (ANOVA, F-test with Greenhouse-Geisser correction for p-values where applicable) using SPSS statistical software. To evaluate significant effects post-hoc t-tests for either paired or independent samples were applied with Bonferroni corrections for multiple comparisons. Time windows were selected differently for each experiment according to the specific question that was addressed. In our first study we were interested in ERP components that peaked around 400 ms after stimulus

presentation ("N400") since this time window has been shown to be sensitive to familiarity (e.g. Mecklinger, 2006). Therefore, mean amplitudes of ERP responses in a time window of 300-600 ms post-stimulus were calculated. In the subsequent second and third studies we chose two time windows to further delineate the visual processing of our stimuli: a fronto-central N350 peaking between 200 and 400 ms and a parietal late positive component (LPC), peaking between 400 and 600 ms after stimulus presentation that are associated with familiarity- (N400) and recollection-related (LPC) recognition effects, respectively.

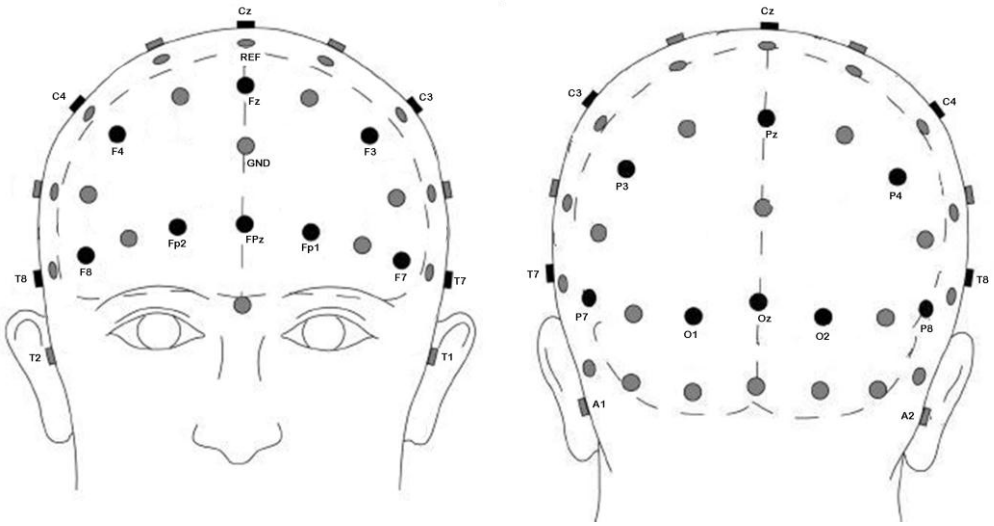

Figure 3. Arrangement of EEG electrodes seen from the front (left) and from the back (right). 23 electrodes (in black) including one reference (REF) and one ground electrode (GND) were used to records ERPs. They were manually placed on the scalp (grey measuring points) according to the international 10/20 system in the case of in-patients, or they were attached in an elastic cap in the case of healthy subjects. Linked mastoid electrodes (A1 and A2) were used for offline re-referencing in post-processing.

3.4.2 Common design features: VOCAP and VOCAPPA

The design of the first two studies was a visual object categorization task in which subjects were asked to press a corresponding button on a computer joypad in order to distinguish pictures of buildings from pictures of every-day life objects. Subjects were placed in a comfortable chair in a sound-proof room with dimmed light to enhance visual contrast and stimuli were presented visually on a computer screen at a distance of 1m from the participants. Subjects were able to choose the correspondence of the buttons according to their own preference. Note that we did not inform our subjects about the two different building categories. Instead, pictures of every-day life objects were introduced as a second category that subjects had to discriminate from the buildings. The total number of stimuli was 240, with 60 pictures

of high- and 60 pictures of low-ranking buildings, and 120 pictures of every-day life objects. The presentation time of the stimuli was 250 ms with an interstimulus interval of 1750 ± 250 ms. All pictures were presented only once in a pseudo-randomized order. After every 60 stimuli there was a break of indefinite length during which participants could have a rest. This was necessary since ERP recordings are very susceptible to muscle-related artifacts like blinks or eye movements.

3.4.3 Specific design features: STEBS

Contrary to the two previous experiments, the third study we termed "study and test of buildings" (STEBS) was used a study-and-test design and consisted of two phases with a short interval in between. During study, participants were asked to memorize 14 pictures of buildings that were presented on a computer screen. After a distraction interval of 30 seconds in which subjects were asked to close their eyes and count backwards from a variable number that appeared on the computer screen the same 14 items were presented again randomly mixed with 14 new pictures. In this test phase subjects had to press a corresponding button whenever they thought the presented item was new or whether they thought they have seen the item before. Again, subjects were able to choose the correspondence of the buttons according to their preference.

A total of 224 drawings of high- and low-ranking buildings with 112 high- and 112 low-ranking pictures was presented. In line with the two previous studies, presentation time of the stimuli was 250 ms and the interstimulus-interval was 1750 ± 250 ms. The STEBS design consisted of a total of 8 trials each lasting about 2 minutes with a total duration of the experiment of less than 20 minutes.

4 ORIGINAL ARTICLES

This doctoral thesis is based on three first authorship articles:

A1 **Oppenheim I.,** Mühlmann H., Blechinger G., Mothersill I.W., Hilfiker P., Jokeit H., Kurthen M., Krämer G., Grunwald T. *Brain Electrical Responses to High- and Low-Ranking Buildings.* Clinical EEG & Neuroscience. 2009; 40(3):157-161.

A2 **Oppenheim I.**, Vannucci M., Mühlmann H., Gabriel R., Jokeit H., Kurthen M., Krämer G., Grunwald T. *Hippocampal contributions to the processing of architectural ranking.* Neuroimage. 2010; 50(2):742-752.

A3 **Oppenheim I.**, Vannucci M., Mühlmann H., Gabriel R., Jokeit H., Krämer G., Grunwald T. *Encoding and recognition of architectural ranking*. 2010. *Manuscript in preparation.*

My contribution to the articles was the planning of the design of the studies, the recruitment of subjects and evaluation of patients, the assessment and analysis of behavioral and neurophysiological data, and writing the drafts and the manuscripts, including revised versions.

All work was done under the supervision of Prof. Dr. Dr. med Thomas Grunwald, head of department of Clinical Neurophysiology, Swiss Epilepsy Centre, Zurich, Switzerland. All EEG measurements were performed at the department of Clinical Neurophysiology at the Swiss Epilepsy Centre in Zurich.

A1) Brain electrical responses to high- and low-ranking buildings

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Published in: *Clinical EEG & Neuroscience. 2009 Jul; 40(3):157-161.*

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Key words:

Event-related potentials, visual processing, familiarity, ranking, design, architecture

ABSTRACT

Since the ancient world architecture generally distinguishes two categories of buildings with either high- or low-ranking design. High-ranking buildings are supposed to be more prominent and, therefore, more memorable. Here, we recorded event-related potentials (ERPs) to drawings of buildings with either high- or low-ranking architectural ornaments and found that ERP responses between 300 and 600 ms after stimulus presentation recorded over both frontal lobes were significantly more positive in amplitude to high-ranking buildings. Thus, ERPs differentiated reliably between both classes of architectural stimuli although subjects were not aware of the two categories. We take our data to suggest that neurophysiological correlates of building perception reflect aspects of an architectural rule system that adjusts the appropriateness of style and content ("decorum"). Since this rule system is ubiquitous in Western architecture, it may define architectural prototypes that can elicit familiarity memory processes.

INTRODUCTION

Functional imaging studies have identified brain areas within the ventral visual pathway that participate particularly in the visual processing of buildings,[1-3] although it is not clear whether these findings suggest the existence of a separate cortical module for building perception.[4] Independent of this question, however, it can be asked which neuropsychological processes can be triggered by architectural stimuli. To know such processes would be helpful if architectural design should utilize neuroscientific results, as suggested e.g. by Goldstein.[5] In fact, it has been known for a long time that familiarity with one's public and private environment can contribute to enhanced quality of life and functional integrity–especially in persons with mild or moderate memory deficits. Thus, from a neuropsychiatric point of view architectural design becomes important because it can provide "prominent local cues that serve to establish uniquely memorable routes (...)" so that "the 'memorability' of an environment can be enhanced, and hence a strong sense of place can be reinforced".[6] However, what exactly makes a building prominent? Size (or deviation from "standard size") may be an important feature, but it seems neither practical nor wise to propose e.g. that architects should design only huge buildings. And although size matters, there have to be other factors, because even a small sacral building may elicit sublime feelings while a huge doghouse may perhaps not. Thus, architectural design has to address questions of "style", which may be difficult to answer using neuroscientific methods. Moreover, to our knowledge, previous experimental studies have searched for brain activations elicited by buildings as such (especially as opposed to activations induced by the processing of faces.[3, 7]), but not for brain regions or processes differentiating between different *kinds* of buildings.

Unnoticed by neuroscientists so far, architectural theory has been addressing the possible prominence of buildings for a long time. At least in Western culture, architectural textbooks from Vitruv's 10 Books on architecture, written between 33 and 22 B.C.,[8] to the books of medieval building lodges and textbooks of the Italian renaissance have described how ornaments should be used to make buildings prominent.[9] Moreover, these ornaments have evolved into a system in which buildings were classified according to the rules of the architectural "decorum", eventually following the Roman law, so that all buildings were designated higher or lower rankings between the poles of the "sublime" and the "low".[10] Those architectural modules and materials that served to signify higher rankings were designed to be outstanding while those associated with the low were not. In general, architectural stimuli indicating higher ranking were reserved for public sacral buildings and constructions associated with matters of military sovereignty while they were not used for buildings associated with economy or the private life.

If this architectural decorum system should indeed have the desired differential effects on the minds and brains of the beholders of buildings then it should make high-ranking buildings more memorable. Thus, ornamental modules traditionally associated with higher ranking should be more familiar even to subjects who have no explicit knowledge of architectural theory. Numerous studies of brain electrical responses to visual and verbal stimuli have shown that the N400-component of event related potentials (ERPs) is sensitive to familiarity, independent of conscious recollection (for a review see e.g.[11]). For example, in "old vs. new" recognition paradigms, N400 amplitudes have been found to be reduced to stimuli that are judged as "old", even when subjects cannot recollect specific details from the study

episode.[12] Moreover, it is hypothesized that this N400 effect reflects implicit rather than explicit memory processes.[13]

Therefore, we hypothesized, that buildings with high-ranking ornaments should elicit N400-potentials that are reduced in amplitude compared to N400-potentials elicited by low-ranking buildings. To test this hypothesis, we recorded ERPs to drawings of buildings with either high-ranking or low-ranking architectural attributes in a visual categorization task.

MATERIALS AND METHODS

Thirteen healthy subjects (seven females; age range 21-58, mean age 31) all born and raised in central Europe participated in this study. Eleven were right- and two were left handed (self-reported) and all had normal or corrected-to-normal vision. None of them had previous training in visual arts or architecture, and none of them reported to be particularly interested in reading books or journals about these fields. All subjects gave informed consent and the study was approved by the local medical ethics committee.

In a sound-proof room with dimmed lights subjects were placed in a comfortable chair facing a computer screen in 1 m distance. ERPs were recorded while the subjects were performing a visual object categorization task in which they were asked to press a corresponding button on a joypad in order to distinguish pictures of everyday life objects from pictures of buildings. Stimuli consisted of 120 different drawings of everyday life objects serving as control condition, and 120 different drawings of buildings (including 60 high- and 60 low-ranking). Every picture was presented only once, and the order of appearance was pseudo-randomised.

Based on the hypothesis that architectural perception is influenced by ranking inference, we designed pictures of buildings representing the two categories *high*- and *low*-ranking, according to the theory of decorum. We classified our stimuli according to the composition and nature of decorated ornamental modules used to construe the fictitious buildings, which we newly produced in order to avoid recognition of buildings existing in reality. The pictures were designed using a matrix consisting of two axes along which we arranged the same architectural attributes according to their supposed ranking (from high to low: archway, Doric, Ionic, Corinthian columns, upright format, landscape format, cottage). Randomly chosen intersections in this array thus determined the composition and nature of ornaments for each newly designed building. Separated by the diagonal of the matrix, buildings designed with more high-ranking attributes were defined as *high*- and those with more low-ranking attributes as *low*-ranking architectural stimuli. Thus, a total of 240 pictures were pseudo-randomly presented with a presentation time of 200 ms and an interstimulus-interval of 1750 ± 250 ms. All stimuli were black-and-white drawings produced by a professional graphic artist for the purposes of this experiment taking specific care of comparable size, contrast, and brightness (for examples of stimuli, see Figure 4). Subjects were asked to differentiate drawings of buildings from those of everyday life objects *and convenience goods,* which served as control condition. We did not inform our subjects about the two categories of buildings.

ERPs were recorded from 23 scalp electrodes according to the international 10/20 system. Data were obtained using a DC amplifier with a sampling rate of 256 Hz per channel. They were offline re-referenced to linked mastoids and bandpass filtered with 0.03-30 Hz (12 dB/ oct). ERP components of 1200 ms duration including a 200 ms pre-stimulus baseline were selectively averaged and manually rejected if

contaminated with artifacts. Only ERPs elicited by correctly identified pictures were included in the average process. Since words and pictures have been shown to elicit a negative ERP component peaking around 400 ms after stimulus presentation ("N400") that are sensitive to familiarity mean amplitudes of ERP-responses in a time-window of 300-600 ms post-stimulus were calculated relative to a 200 ms pre-stimulus baseline. For statistical analysis, mean amplitudes of ERPs to high- and to low-ranking buildings were subjected to a repeated measures analysis of variance (ANOVA, F-test with Greenhouse-Geisser correction for p-values where applicable) using SPSS statistical software. We considered only recordings from frontal, temporal, central and parietal contacts (F3, F4, F7, F8, T3, T4, C3, C4, P3, P4, Fz, Cz, Pz) and calculated an ANOVA first with the within-subject factors *stimulus type* (high *vs* low) and *electrode* (n = 13). To test differential responses of the two hemispheres we additionally calculated an ANOVA with the within-subject factors *stimulus type* (high *vs* low), *side* (left *vs* right) and *electrode* (n = 10, with the lateralized contacts F3, F7, T3, C3, P3 for the left side, and F4, F8, T4, C4, P4 for the right side).

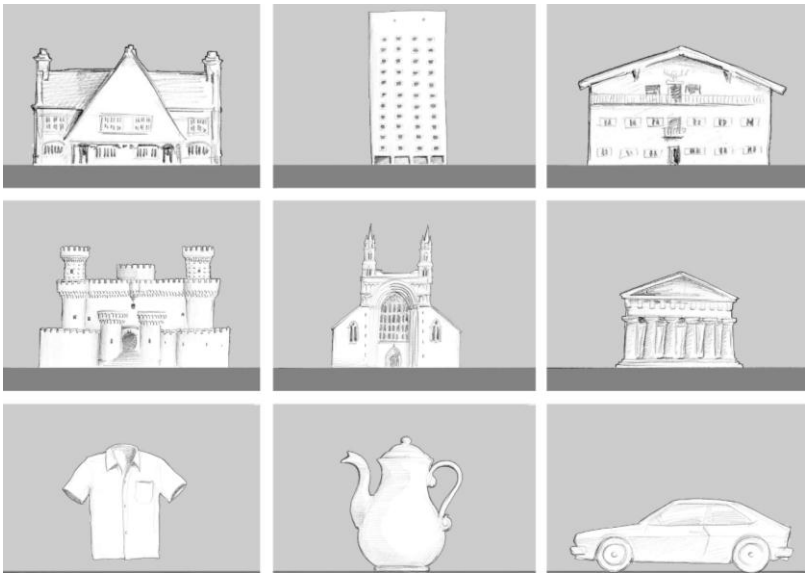

Figure 4. Examples of the pictures used as stimuli showing low-ranking buildings (upper row), high-ranking buildings (middle row) and objects (lower row).

RESULTS

Subjects correctly classified 98.26 ± 1.62 % (mean ± s.e.m.) of the objects, 97.94 ± 3 % of the high-ranking and 98.22 ± 1.6 % of the low-ranking buildings. Likewise there were no significant differences between response times to objects (687.51 ± 77.65 ms), high-ranking (714.61 ± 59.98 ms) and low-ranking buildings (711.27 ± 60.8 ms).

Both high- and low-ranking buildings elicited N400-like responses especially over frontal electrode contacts (see Figure 5). Repeated measures ANOVA revealed significant effects of both *stimulus type* ($F_{1,12} = 18.82$, $p < 0.005$) and *electrode* ($F_{12,12} = 11.27$, $p < 0.001$) on mean amplitudes of ERP responses to buildings in the time window of 300–600 ms after stimulus presentation as well as a significant interaction of both factors ($F_{1,12} = 4.264$, $p < 0.05$), indicating more positive-going ERP waveforms to high-ranking than to low-ranking buildings especially over frontal electrode contacts. Post-hoc t-tests for paired samples with Bonferroni corrections for repeated comparisons showed that mean amplitudes of ERP responses to low-ranking buildings were significantly more negative than those to high-ranking buildings (low *vs* high: F3: -3.8 *vs* -1.0 ; Fz: -2.8 *vs* -0.4; F4: -2.3 *vs* 0.3; F7: -4.1 *vs* -1.9; F8: -2.6 *vs* -1.3 µV; $p < 0.01$ for all contacts). An additional repeated measures ANOVA with the third factor *side* (left *vs* right) confirmed the significant effects of both *stimulus type* ($F_{1,12} = 18.16$, $p < 0.005$) and *electrode* ($F_{4,12} = 12.00$, $p < 0.005$) and showed a significant effect of the factor *side* ($F_{1,12} = 18.15$, $p < 0.005$). Although this indicated somewhat higher mean amplitudes to buildings over the left hemisphere, we found no significant interaction between the factors *stimulus type* and *side,* thus indicating that both hemispheres differentiated similarly between high- and low-ranking buildings.

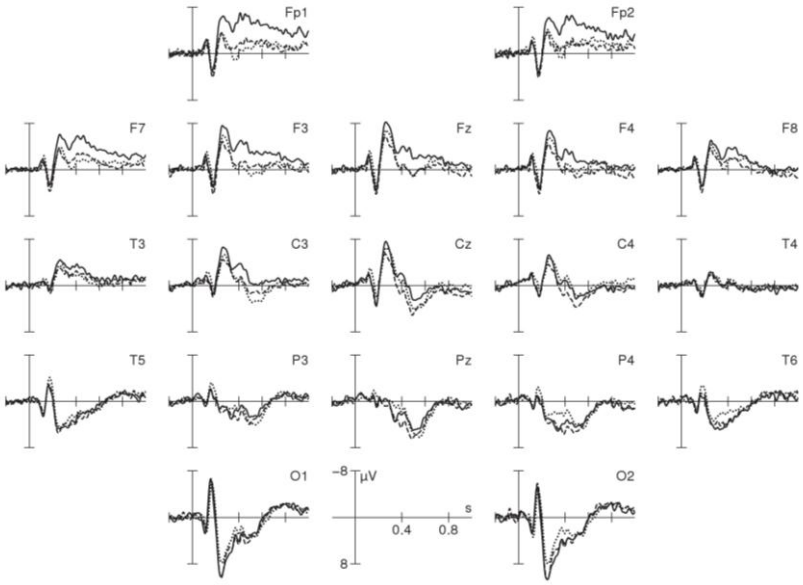

Figure 5. Grand averages of event-related potentials recorded in 13 participants. Waveforms show responses to low-ranking buildings (solid line), high-ranking buildings (dashed line), and objects (dotted line). Negative amplitudes are plottted upwards. Note that the P110-, N160-, and P250-components evoked by high- and low-ranking buildings in O1 and O2 overlap.

Concordantly, repeated measures ANOVA considering all three stimulus types (high- vs. low-ranking buildings vs. objects) showed significant effects of both *stimulus type* ($F_{2,12} = 12.65$, $p < 0.001$) and *electrode* ($F_{12,12} = 9.48$, $p < 0.001$), as well as a significant interaction of both factors stimulus type x electrode ($F_{1,12} = 7.04$, $p < 0.001$). As Figure 5 shows, N400s to low-ranking building differed considerably from those to objects while N400s to high-ranking-buildings and objects appeared similar. Therefore, we calculated a further repeated measures ANOVA for these two stimulus types (high-ranking buildings vs. objects). While there was no significant effect of *stimulus type* ($F_{1,12} = 1.04$, n.s.), effects of *electrode* ($F_{4,12} = 5.57$, $p < 0.05$) and *side* ($F_{1,12} = 6.06$, $p < 0.05$) were significant. However, there was a significant interaction between *stimulus type* and *side* ($F_{1,12} = 30.11$, $p < 0.001$), indicating that both hemispheres differentiated unequally between high-ranking buildings and objects. Post-hoc t-tests for paired samples with Bonferroni corrections for repeated comparisons showed that the difference between mean

N400-amplitudes to high-ranking buildings and objects was larger on the right side at frontal and central sites (F4 vs. F3: 0.95 vs. -0.76 mA, $p < 0.005$; C4 vs. C3: 2.07 vs. -0.78 mA, $p < 0.005$). As these differences indicate and as can be seen in Figure 5, responses to high-ranking buildings at F4 and C4 were even more positive-going than those to objects.

Prominent in recordings from the occipital contacts O1 and O2, both high- and low-ranking buildings elicited early components peaking around 110 ms ("P110"), 160 ms ("N160"), and 250 ms (P250), which are associated with visual processing. Repeated measures ANOVA with the within-subject factors *stimulus type* (high vs low) and *side* (O1 vs O2) revealed no significant effects of either stimulus type (P110: $F_{1,1} = 2.61$, n.s.; N160: $F_{1,1} = 1.18$, n.s.; P250: $F_{1,1} = 3.43$, n.s.) or electrode: (P110: $F_{1,1} = 0.28$, n.s.; N160: $F_{1,1} = 1.87$, n.s.; P250: $F_{1,1} = 3.33$, n.s.). Neither did these two factors interact significantly for any of these components.

DISCUSSION

Architectural theory holds that buildings can be designed to be perceived as either high- or low-ranking, at least in Western architectural styles adhering to the rules of the classical decorum. Ornaments designating a building as high-ranking are thought to make these buildings more prominent and therefore more memorable. If this conjecture was true, high-ranking architectural designs should be more familiar at least to subjects born and raised in cultures that have been using the classical Western decorum for centuries. We set out to test this claim by recording ERPs to drawings of fictitious buildings with either high-ranking or low-ranking architectural ornaments. Indeed, we found that ERP responses recorded over both frontal lobes

differentiated reliably between both classes of architectural stimuli, although subjects reported after the experiment that they were not aware of the two categories. More precisely, high-ranking buildings elicited N400-potentials that were significantly lower in amplitude than those to low-ranking buildings. We take this finding to indicate that architectural ornaments traditionally judged as high-ranking indeed elicit a greater sense of familiarity than low-ranking ornamental modules.

Of course, alternative interpretations of our data have to be considered. However, the black-and-white drawings of these stimuli were controlled for size, contrast and brightness so that is unlikely that perceptual differences can account for our findings. This view is also supported by the practically identical early visually evoked potentials recorded over both occipital lobes (see Figure 5).

On the other hand, it might be argued that high-ranking buildings may be perceived as more beautiful, thus speculating whether other graphical features of the stimuli could explain our findings. Especially, symmetry[14] and stimulus complexity[15, 16] have been found to influence aesthetic judgments of beauty. However, because of the chosen strategy of the design explained above, the number (but not nature) of ornaments was comparable in high- and low-ranking buildings. Because of the same reason, symmetry was equally present or absent in the drawings of both classes of buildings.

Since it was the nature (i.e. Doric vs. Corinthian columns etc.) but not number of ornaments that differentiated high- and low-ranking buildings in our set of stimuli,

it could also be argued that the latter may have been perceived as less beautiful on other grounds than those of complexity and symmetry. Therefore, low-ranking buildings might have elicited more negative-going ERPs. In fact, Jacobsen and Höfel (2003) found that graphic patterns judged as not beautiful elicited a phasic negativity in the time-window of 300–400 msec after stimulus onset that was higher in amplitude compared to ERPs elicited by patterns judged as beautiful.[14] The scalp topography of this negative deflection to non-beautiful patterns suggested an involvement of the frontal cortex–a hypothesis also supported by fMRI-data.[17] At first sight, our data seem to be concordant with these findings: Compared to high-ranking buildings, low-ranking buildings elicited more negative-going ERPs in the time-window of 300–600 ms after stimulus-presentation over frontal brain areas. However, Höfel and Jacobsen (2007) found that an early frontocentral negativity for less attractive patterns could not be elicited in tasks not requiring an overt aesthetic judgment, which our task did not.[18] In addition, Höfel and Jacobsen showed in the same study that processes of evaluative categorization were associated with a lateralized late positivity between 500 and 770 ms after stimulus onset that could only be elicited when the aesthetic value of graphic patterns had to be evaluated. Several other studies found a late positive potential (LPP) associated with evaluative categorization and peaking maximally at centroparietal electrodes.[19, 20] We recorded no such late positivity in our object categorization task that did neither require evaluative categorizations nor aesthetic judgments. Taken together, these data of earlier studies suggest that our finding of more negative-going ERPs to low-ranking buildings between 300 an 600 ms after stimulus presentation does not necessarily reflect the aesthetic inferiority of these stimuli.

We suggest that, as hypothesized, the differentiation between brain electrical responses to high- and low-ranking buildings observed here was influenced by memory processes, because high-ranking buildings elicited N400-like components that were lower in amplitude than N400-like responses to low-ranking buildings. Of course, it could be argued that perception of low-ranking buildings might be associated with novelty detection and therefore increased N400 amplitudes (e.g.[21]). However, since low-ranking buildings typically represent "normal", "everyday" buildings associated with economy or the private life, it is hard to conceive how these stimuli should elicit specific novelty effects. In fact, most buildings encountered in daily life are low-ranking and should therefore be more familiar instead of more novel than high-ranking buildings. Moreover, no fronto-central positivity, which has been associated with novelty detection (e.g.[22, 23]) was elicited by low-ranking buildings. Conversely, it seems more likely that buildings distinguished by high-ranking ornamental modules are easier to encode and thus create more lasting memories. Concordant with this hypothesis, we found reduced N400 amplitudes especially over frontal electrode contacts, thus resembling the well-known mid-frontal effect of familiarity on brain electrical ERP responses (e.g.[24]). Note, however, that our findings do not suggest that only high-ranking ornaments can make a building memorable. In contrast, deviation from standards–and thus novelty–can be a powerful stimulus for encoding into declarative/episodic memory.

Our drawings of high-ranking buildings were artificially designed and did not depict existing architecture. Nor did any subject report on request that he or she "recognized" any of the presented buildings. Thus, if familiarity played a role in our findings, the associated memories cannot have been episodic but may, perhaps, refer to "prototypes" of buildings characterized by specific high-ranking ornaments.

If this was the case, it can also be asked whether "prototypical" high-ranking buildings are easier to verbalize. It cannot be excluded that high-ranking architectural designs are more likely to trigger semantic processes than low-ranking buildings. At least for intrahippocampal ERP recordings it has been shown that verbalizable pictures elicit positive-going ERP responses that nonsense-objects do not.[25, 26] Supporting this hypothesis is the observance that ERPs for the high-ranking buildings were much more similar (although not identical) to the ERPs elicited by the easily nameable everyday life objects that we used as control stimuli. That brain electrical responses to objects were more different from those to low-ranking than from those to high-ranking buildings suggests that the enhanced frontal negativity to low-ranking buildings cannot be explained by their distinction as a building alone. However, the similarity (though not identity) of responses to high-ranking buildings and objects indicates that further studies are needed to analyze the neuropsychological processes involved in the perception of architectural stimuli more closely. However, since our architectural stimuli differed only in the nature of their ornaments, we suggest that high-ranking ornaments can help to facilitate the visual processing of buildings–either by making them semantically classifiable or by eliciting familiarity memory processes.

In sum, we take our findings to suggest that the perception of architectural design is sensitive to rules of the classical decorum system, at least in persons born and raised in Western cultures. This hypothesis predicts that it should not be possible to find the same N400-effects of Western high- and low-ranking architectural ornaments in persons who have no knowledge of and experience with the Western decorum system–a prediction which future studies may want to test. Thus, our data indicate

that the arts and neurosciences can well ally to generate predictions that can be tested with neuroscientific methods.

ACKNOWLEDGMENTS

We thank Rainer Gabriel for the production of the pictures that were used as stimuli and Manila Vannucci for helpful comments and suggestions.

DISCLOSURE

Ilan Oppenheim has designed and created the experiment, recruited and informed all participants, obtained ERP data, carried out ERP post-processing and statistical analysis, and written the draft and the manuscript of this article.

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A2) Hippocampal contributions to the processing of architectural ranking

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Published in: *Neuroimage. 2010 Apr 1;50(2):742-52. Epub 2010 Jan 4.*

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Key words: Event-related potentials, visual processing, hippocampus, temporal lobe epilepsy, architecture, decorum

ABSTRACT

Theories of rhetoric and architecture suggest that buildings designed to be high-ranking according to the Western architectural decorum have more impact on the minds of their beholders than low-ranking buildings. Here, we used event-related potentials in a visual object categorization task to probe this assumption and to examine whether the hippocampus contributes to the processing of architectural ranking. We found that early negative potentials between 200 and 400 ms differentiated between high- and low-ranking buildings in healthy subjects and patients with temporal lobe epilepsy with and without hippocampal sclerosis. By contrast, late positive potentials between 400 and 600 ms were higher in amplitude to high-ranking buildings only in healthy subjects and TLE patients without but not in TLE patients with hippocampal sclerosis. These findings suggest that the differentiation between high- and low-ranking buildings entails both early visual object selection and late post-model selection processes and that the hippocampus proper contributes critically to this second stage of visual object categorization.

INTRODUCTION

Winston Churchill coined the famous quote "We shape our buildings, and afterwards our buildings shape us" (Churchill, 1943). If he was right, then buildings must leave their marks in our memory, and it should be possible to find traces of these marks with neurophysiological methods. Indeed, we recently found that brain electrical responses differentiate between buildings characterized by architectural ornaments as being more important or "high-ranking" and buildings designed to be comparably less important or "low-ranking" (Oppenheim et al., 2009). Ranking of architectural ornaments and buildings follows–at least in Western cultures–rules of the architectural decorum. From Vitruv's 10 Books on architecture, written between 33 and 22 B.C. (Vitruvius, 1999) to Alberti's "10 Books on Architecture", written in the middle of the 15th century (Alberti, 1485) and Vignola's most famous book "Rule of the Five Orders" (Vignola-Barozzi 1582) and into modernity architectural ornaments have evolved into a system in which buildings are designated higher or lower rankings between the poles of the "sublime" and the "low" (Mühlmann, 1996). In general, architectural stimuli indicating higher ranking were reserved for public sacral buildings and constructions associated with matters of political and military sovereignty while they were not used for buildings associated with economy or the private life. The Alberti-Vignola system represented the major influence on architecture until the beginnings of the 20th century. European inner cities are characterized by Vignolian architecture, and even during the 20th and early 21st century ornaments and ranking have remained central topics in architectural design.

In a recent study we found that event-related potentials (ERPs) peaking about 400 ms after stimulus presentation were significantly more positive in amplitude when they were elicited by pictures of high- as compared to low-ranking buildings

(Oppenheim et al., 2009), suggesting that visual perception of architectural design is sensitive to rules of classical decorum system (at least in subjects born and raised in Western cultures). Thus, visual encounters with high-ranking buildings may leave traces of their cultural prominence in the beholder's memory that facilitate visual-semantic processing of high- as compared to low-ranking buildings. That visual and memory processes are linked within the human hippocampus has been shown by recordings of hippocampal ERPs that some members of our group were able to record during tests of visual processing in TLE patients undergoing invasive presurgical evaluations with medial temporal depth electrodes; they observed that a late positive component (LPC) or P600 differentiated reliably between real and nonsense objects (Vannucci et al., 2003) and between identified and unidentified visual objects (Vannucci et al., 2006) only within intact but not in epileptic hippocampi. Moreover, they found the normal hippocampal differentiation between real and nonsense objects only in patients with normal visual memory but not in patients whose visual memory performance was reduced (Vannucci et al., 2008). In addition, the hippocampal LPC or P600 has also been shown to be larger in amplitude to famous than to unfamiliar faces (Trautner et al., 2004; Dietl et al., 2005), and it is larger to words with high than to words with low imageability (Klaver et al., 2005). These findings suggest that the human hippocampus contributes to the semantic (and perhaps associative) processing of visual and visualizable verbal stimuli and that these contributions are directly linked to visual memory performance. Therefore, the aim of the present study was to examine whether and how the hippocampus contributes to the differentiation between high- and low-ranking buildings and whether this process is impaired in patients suffering from medial temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS).

Late positive components associated with visual processing have also been found in ERP recordings from the scalp: a series of studies by Schendan and Kutas (2002, 2003, 2007a, 2007b) on visual object categorization shows (in agreement with numerous studies cited therein) that visual object processing and categorization encompasses–after initial perceptual processes–an earlier state during which a perceived object is matched to visual knowledge in long-term memory so that a class of objects can be selected to which the percept may belong. This *object model selection* is associated with a fronto-central ERP component peaking around 350 ms after stimulus presentation (N350). The N350 is modified by perceptual and conceptual implicit memory processes (Schendan and Kutas, 2003, 2007a, Schendan and Maher, 2009) and by perceptual expertise (Schendan and Kutas, 2003) and may depend on contributions of the temporal lobe (Löw et al., 2003). In fact, these studies indicate that the fronto-central N350 seems to be a complex of distinct ERP subcomponents peaking at different latencies and sites and reflecting the hierarchical activation of different but interacting "perceptual" knowledge (specifically related to the visual structure of the object) and more abstract and conceptual kinds of object knowledge. Following successful object model selection, the activation of associated knowledge may support finding a name (*post-model selection* processes) and recollecting earlier encounters with the perceived object. This later state of visual object categorization is associated with a parietal late positive component (LPC) including a P600 and may also tap aspects of explicit (episodic) memory processes (Schendan and Kutas, 2007a; Schendan and Maher, 2009).

It is tempting to relate hippocampal LPCs to those recorded with scalp electrodes. However, because the hippocampus proper may electrically be a closed field, at least in part (Klee and Rall, 1977), ERPs generated within the hippocampus are attenuated in extrahippocampal recordings (Grunwald et al., 1999). Nevertheless, parahippocampal laminar cortical structures may well contribute to scalp ERPs. But even if hippocampal and scalp LPCs were related, it would be impossible to decide from these depth recordings alone whether the hippocampus contributes or reacts to those subprocesses of visual object categorization that are associated with LPCs recorded from the scalp. However, if it can be shown that hippocampal sclerosis interferes with ERP components in the LPC time-window then we could conclude that the hippocampus proper contributes to the associated neuropsychological processes at least in part. To this aim we recorded scalp ERPs in healthy subjects and TLE patients with (HS+) and without hippocampal sclerosis (HS–) in a visual object categorization task using pictures of high- and low-ranking buildings and everyday life objects.

MATERIALS AND METHODS

Patients and healthy subjects

A total of 30 TLE patients volunteered to participate in the study (15 females; mean age 39.9 years; age range 18–57). Twenty-five patients were right-handed (self-reported), and functional magnetic resonance imaging indicated left-sided language dominance in all 5 left-handed patients. In all patients diagnosis of unilateral TLE with partial and/or secondary generalized tonic clonic seizures was based on typical clinical seizure semiology, interictal and ictal EEG findings and the results of MRI scans (for clinical data see Table 1). MRI scans indicated unilateral hippocampal

sclerosis (HS) in 20 patients (10 left, 10 right). Only patients with no additional (e.g. extrahippocampal) damage were included in this group. Six patients had different lesions within the temporal lobe (e.g. parahippocampal, amygdala) not affecting the hippocampus while in four patients no abnormalities were detected. One of the patients with left-sided hippocampal sclerosis had to be excluded because of technical problems during ERP recordings. To study the effect of hippocampal sclerosis on the differentiation between high- and low-ranking buildings we thus included 9 patients with left-sided (LTE) and 10 with right-sided medial temporal lobe epilepsies (RTE) with unilateral HS (HS+ group). The remaining 10 TLE patients without MRI signs of hippocampal pathology (4 left and 6 right) were considered for additional comparisons (HS– group) (see Table 2).

All except one patient were treated with antiepileptic drugs (AEDs) during the recording of this study. In the patient without prior drug treatment, antiepileptic medication was initiated during the period of the experiment. Both in HS+ and in the HS– patients lamotrigine (n = 11 (HS+) vs. n = 5 (HS–)) and levetiracetam (n = 10 (HS+) vs. n = 4 (HS–)) were the most frequently used AEDs. Most patients were either on a AED monotherapy (n = 8 (HS+) vs. n = 5 (HS–)) or received two drugs in combination (n = 7 (HS+) vs. n = 4 (HS–)). Following our inclusion criteria, none of the patients experienced a seizure in a 24 h period preceding the experimental session. There was no group difference between all LTE (n = 14) and RTE (n = 16) patients with regards to age (mean ± s.d.: 36.2 ± 10.8 vs. 41.9 ± 9.6 years), duration of epilepsy (21.3 ± 21.2 vs. 26 ± 13.8 years) or age at seizure onset (15 ± 15.5 vs. 15.9 ± 11 years). The same holds true for the comparison between HS+ (n = 20) and HS– (n = 10) patients where there was also no difference with regards to age (39.5 ± 11.2 vs. 39.6 ± 9.6 years; p = 0.09), duration of epilepsy (24.2 ± 13.7 vs. 22.7 ± 9.7 years) or age at seizure onset (14.2 ± 14.8 vs. 15.9 ± 9.1 years) (for behavioral and demographic data see Table 3).

Fourteen healthy subjects (7 females; one left-handed) with a mean age of 42 years (range 26–64) participated as control group. The mean age of healthy participants and TLE patients did not differ significantly (42.3 ± 12.8 vs. 39.2 ± 10.4 years). All subjects and patients participating in this study were born and raised in Central Europe, had normal or corrected-to-normal vision (i.e., wearing glasses or contact lenses), and none of them had any skull defects or had undergone any neurosurgical procedures. None of them had previous training in visual arts or architecture, and none of them reported to be particularly interested in reading books or journals about these fields. All subjects gave informed and written consent. The study was approved by the local medical ethics committee and was in compliance with the Declaration of Helsinki.

Table 1. Clinical data of TLE patients with hippocampal sclerosis.[a]

Patient	Sex	Handedness	Age	Years of epilepsy	Side of TLE	MRI-findings
8	M	RH	25	22	Left	HS
11	F	RH	36	33	Left	HS
16	M	LH	35	31	Left	HS
19	F	LH	26	21	Left	HS
25	M	RH	20	15	Left	HS
29	F	RH	46	45	Left	HS
33	F	RH	44	24	Left	HS
38	F	RH	43	5	Left	HS
40 [b]	M	RH	18	8	Left	HS
45	M	RH	57	2	Left	HS
3	F	RH	43	40	Right	HS
5	M	RH	49	27	Right	HS
22	M	LH	41	36	Right	HS
31	F	RH	46	42	Right	HS
37	F	RH	36	8	Right	HS
46	M	RH	45	33	Right	HS
48	F	RH	24	3	Right	HS
49	F	RH	47	22	Right	HS
51	M	LH	53	50	Right	HS
52	M	RH	47	17	Right	HS

[a] RH, right-handed; LH, left-handed; HS, hippocampal sclerosis; [b] Excluded from ERP analysis.

Table 2. Clinical data of TLE patients without hippocampal sclerosis.[a]

Patient	Sex	Handedness	Age	Years of epilepsy	Side of TLE	MRI-findings
12	M	RH	37	14	Left	N.a.d.
15	M	RH	43	24	Left	Dysplasia of amygdala
20	M	RH	37	16	Left	Lateral temporal gliosis
39	F	RH	40	28	Left	N.a.d.
17	F	RH	53	22	Right	N.a.d.
26	M	RH	32	31	Right	Dysplasia of amygdala
41	M	RH	46	32	Right	Lateral temporal ischemia
42	F	RH	53	35	Right	N.a.d.
43	F	LH	26	3	Right	Dysplasia of amygdala
44	F	RH	29	22	Right	Lateral temporal cavernoma

[a] RH, right-handed; LH, left-handed; N.a.d., no abnormality detected

Table 3. Behavioral and demographic data of left and right TLE patients with and without hippocampal sclerosis.[a]

	HS+	HS–	LTE	RTE	Controls
Number of subjects	20	10	14	16	14
Age [y]	39.5 ± 11.2 a	39.6 ± 9.6	36.2 ± 10.8	41.9 ± 9.6	39.2 10.4
Duration of epilepsy [y]	24.2 ± 13.7	22.7 ± 9.7	21.3 ± 21.2	26 ± 13.8	–
Response time [ms]					
High-ranking buildings	719.52 ± 64.6	719.4 ± 57.01	727.05 ± 46.16	712.91 ± 72.74	756.53 ± 81
Low-ranking buildings	711.49 ± 64.87	718.82 ± 56.78	726.03 ± 45.18	703.35 ± 72.55	752.06 ± 80.43
Objects	692.75 ± 76.53	688.58 ± 59.53	706.47 ± 65.47	678.14 ± 73.74	738 ± 88.3
Accuracy [% correct responses]					
High-ranking buildings	91.72 ± 5.83 t = 4.86 b, **	89.52 ± 13.95	91.28 ± 9.16 t = 2.85 *	90.73 ± 9.43 t = 3.18 *	98.33 ± 1.5
Low-ranking buildings	91.73 ± 8.53 t = 2.91 **	89.99 ± 9.95	90.42 ± 9.56	91.79 ± 8.53	97.62 ± 2.5

[a] Mean values ± standard deviation; LTE, left temporal lobe epilepsy; RTE, right temporal lobe epilepsy; HS+, hippocampal sclerosis; HS–, extrahippocampal temporal lesion; t values reported where significant, all p values after Bonferroni Correction; [b] Contrasts vs. healthy subjects; **, $p < 0.005$; * $p < 0.02$

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Stimuli and task

According to the decorum-rule system ranking inference influences the perception of architectural stimuli. Following the injunctions of the decorum system we designed pictures of buildings representing the two categories of "high-" and "low"-ranking, taking care that these newly designed buildings were not identical with buildings existing in reality and thus with possible contents of the subjects' episodic memories. We classified our stimuli according to the composition and nature of decorated ornamental modules and arranged these modules according to their supposed ranking postulated by the decorum system (from high to low: archway, Doric, Ionic, Corinthian columns and temple facades, upright format of facades, landscape format of facades, cottage) along both axes of a matrix. Randomly chosen intersections in this array thus determined the composition and nature of ornaments for a building. Along the diagonal of the matrix, buildings characterized by more high-ranking attributes were defined as "high-" and those with more low-ranking attributes as "low-ranking" architectural stimuli (Oppenheim et al., 2009). By this method, drawings of a total of 120 buildings (60 high- and 60 low-ranking) were produced. Another 120 pictures of normal everyday life objects were designed and served as second target ("objects") for the task. All stimuli were black-and-white drawings produced by a professional graphic artist for the purposes of this experiment, taking specific care of comparable size, contrast, and brightness (for examples of stimuli, see Figure 6).

Thus, during the experiment a total of 240 pictures were presented only once in a pseudo-randomized order with a presentation time of 200 ms and an interstimulus interval of 1750 ± 250 ms using Eevoke presentation software (release 3.1.5; Elicitor GmbH, Zurich, Switzerland). The experiment was divided into 4 trials with 60 stimuli each, separated by short breaks. We asked our participants to differentiate drawings of buildings from those of everyday life objects by pressing a corresponding button of

a joy pad and did not inform our subjects about the two categories of buildings. To test whether subjects could perform the task we examined correct responses to everyday life objects and buildings. Response times were recorded, although we did not ask our subjects to respond to the stimuli as fast as possible.

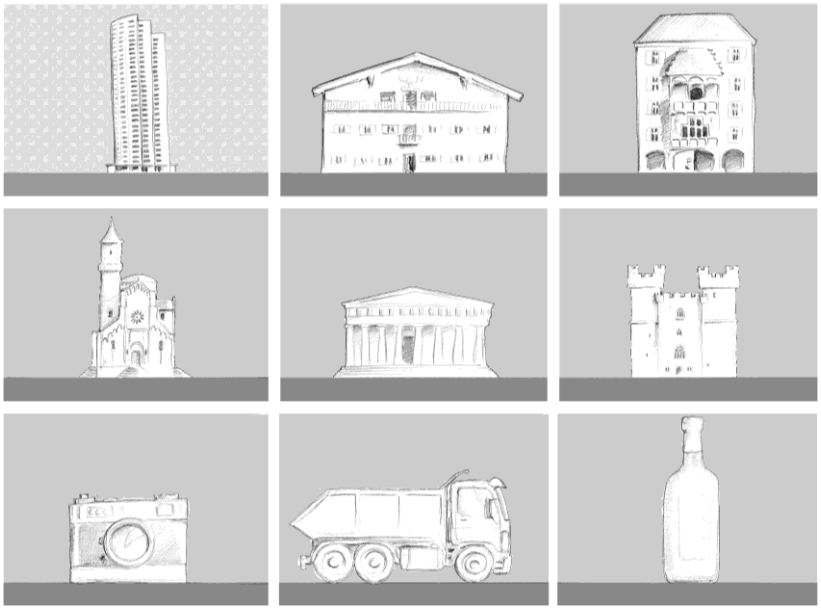

Figure 6. Examples of stimuli used in the experiment showing low-ranking buildings (upper row), high-ranking buildings (middle row) and objects (lower row).

ERP recordings and statistics

Subjects were placed in a comfortable chair in a sound attenuated room with dimmed lights facing a portable computer screen in 1 m distance. Those patients who were not allowed to leave beds during video-/EEG-monitoring performed the visual object categorization task in their beds sitting in an upright position. In all patients and subjects 23 electrodes (including one reference and one ground electrode) were placed according to the international 10/20 system. Midline electrode locations were Fz, Cz, and Pz, and left and right hemisphere sites were Fp1/Fp2, F3/F4, F7/F8, C3/C4, T3/T4, P3/P4, T5/T6, and O1/O2. Using a DC amplifier

(ANT Advanced Neuro Technology, Enschede, The Netherlands), EEGs were recorded continuously with a sampling rate of 256 Hz per channel with scalp impedance always kept below 5 kΩ. Data were band-pass filtered offline with 0.3–30 Hz with 12 dB/oct and re-referenced to linked mastoids. EEG epochs of 1400 ms duration including a 200 ms pre-stimulus baseline were selectively averaged time-locked to the onset of the stimuli. Epochs were inspected visually and rejected in case of false or missing reactions or when ERP signals were contaminated by epileptiform potentials, blinks, eye movements, or other muscle-related artifacts. Only ERP components elicited by correctly classified pictures were included in the average process. ERP components were identified by visual inspection and quantified by peak latency and mean amplitude measurements. We required a minimum of 20 clean trials per subject and stimulus class (maximum = 60). Many epochs were not contaminated by artifacts or epileptiform potentials: on average, 5.9% of the trials (i.e. 14 of 240) were rejected in control subjects, 7.7% (18.5) in the HS+, and 10.6% (25.4) in the HS– group. In a few subjects and patients more trials had to be rejected. However, since the minimal number of valid trials per stimulus class was 39 in healthy subjects, 26 in the HS+ and 22 in HS– group, the responses of all subjects and patients to all stimulus classes met our inclusion criterion for the adequate number of clean trials.

Because visual object processing has been shown to be associated with a fronto-central N350 as well as a parietal LPC, mean amplitudes of ERP responses in the time-window of 200–400 and 400–600 ms post-stimulus were calculated relative to a 200 ms pre-stimulus baseline. We chose time windows of this width because it cannot be excluded that antiepileptic drugs can induce a latency jitter of ERP peak latencies (Puce at al., 1994). Since we were interested in neurophysiological

correlates of the processing of architectural ranking and did not specifically probe visual object categorization and memory, we cannot simply presuppose that the ERP components we recorded are identical with N350s and LPCs as described in the studies by Schendan and Kutas cited above. For this reason we will refer to ERPs recorded in the 200–400 ms time-window as "early negative potentials" (ENPs) and to those recorded in 400–600 ms time-window as "late positive potentials" (LPPs, see Figure 7).

Mean amplitudes of ERPs in the two time-windows were subjected to repeated measures analyses of variance (ANOVA, F-test with Greenhouse-Geisser correction for p-values where applicable) using SPSS statistical software (release 15.0 for Windows; SPSS Inc., Chicago, USA). For ENPs we considered recordings from frontal (F3/F4), frontotemporal (F7/F8) and central contacts (C3/C4), while for LPPs recordings from central (C3/C4) and parietal contacts (P3/P4) were considered. To evaluate significant effects, post-hoc *t* tests for either paired or independent samples were applied with Bonferroni corrections for multiple comparisons.

RESULTS

On average, all participants correctly classified (mean ± standard deviation) 95.42% ± 5% of the objects, 93.52% ± 7.9% of high-ranking buildings, and 93.52% ± 8.3% of low-ranking buildings. To test whether correct responses to the stimuli differed between the three groups (normal controls, HS+, and HS–) we first conducted a repeated-measures ANOVA with the within-subjects factor STIMULUS (objects vs. high-ranking buildings vs. low-ranking buildings) and the between-subjects factor PATHOLOGY (healthy subjects vs. HS+ vs. HS–). This showed a significant

influence of the factor PATHOLOGY ($F[2,40] = 4.72$; $p < 0.05$), but no effect of STIMULUS ($F[2,40] = 2.2$; $p = 0.07$), and no interaction between the two factors. Post-hoc *t* tests revealed that this significance was due to better performances of healthy subjects compared to patients with HS for high-ranking buildings (98.33% ± 1.5% vs. 91.72% ± 5.8%; $p < 0.005$), low-ranking buildings (97.62% ± 2.5% vs. 91.73% ± 8.5%; $p < 0.005$), and objects (97.97% ± 1.7% vs. 93.81% ± 5.2%; $p < 0.005$), while there was no difference in the performance between normal controls and patients without HS. An additional ANOVA including all TLE patients (HS+ and HS–) with the between-subjects factor FOCUS (14 left vs. 16 right) showed that the side of the primary epileptogenic zone had no influence on the patients' performance ($F[1,28] = 0.01$; $p = 0.98$).

Although we did not ask our subjects to respond to the stimuli as quickly as possible, response times were collected and subjected to a repeated-measure ANOVA with the between-subjects factor PATHOLOGY (healthy subjects vs. HS+ vs. HS–). Here we found a significant effect of the factor STIMULUS ($F[2,40] = 8.56$; $p < 0.005$), while there was no influence of PATHOLOGY ($F[2,40] = 1.62$; $p = 0.19$), and no significant interaction between both factors. Post-hoc *t* tests showed that responses to objects (706.44 ± 12.11 ms) were faster than to low-ranking buildings (727.46 ± 10.76 ms; $p < 0.01$) and than high-ranking buildings (731.85 ± 10.8 ms; $p < 0.05$). Again, there was no influence of the side of the epileptogenic focus ($F[1,27] = 1.1$; $p = 0.34$).

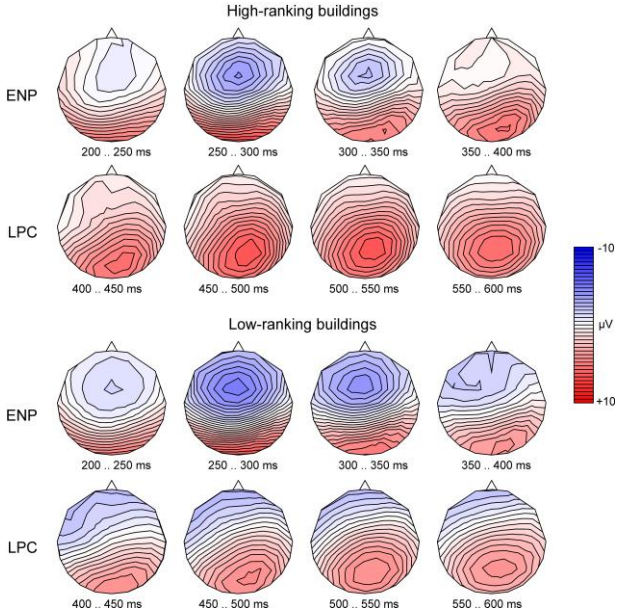

Figure 7. Topographic maps showing the scalp distribution of ERPs to high- and low-ranking buildings between 200 and 600 ms after stimulus presentation in fourteen healthy subjects. ENP, early negative potential; LPC, late positive component.

Early negative potentials (ENPs) in the 200–400 ms time-window

All classes of stimuli elicited early negative potentials (ENPs) peaking around 330 ms after stimulus presentation over frontal (F3, F4), frontotemporal (F7, F8) and central electrode contacts (C3, C4) (see Figure 8). Since we were especially interested in the differentiation between high- and low-ranking buildings and to test whether these potentials differed between patients with left- and right-sided TLE with and without HS, we submitted mean amplitudes of these components from 200–400 ms of TLE patients to a repeated-measures ANOVA with the within-subjects factors STIMULUS (high- vs. low-ranking buildings), SITE (frontal vs. frontotemporal vs. central), and HEMISPHERE (left vs. right) and the between-subjects factors FOCUS (LTE vs. RTE) and HS (HS+ vs. HS–). The within-subjects factor STIMULUS proved to be significant ($F[1,25] = 27.98$; $p < 0.0005$) as did the between-subjects factor FOCUS ($F[1,25] = 5.61$; $p < 0.05$) but not the between-subjects factor HS ($F[1,25] = 1.04$; $p = 0.32$). While HS did not interact with STIMULUS, there was a significant

interaction between STIMULUS and FOCUS ($F[1,25] = 4.65$; $p < 0.05$) as well as an interaction between STIMULUS x FOCUS x HS ($F[1,25] = 8.83$; $p < 0.01$) indicating that the side of the epileptogenic focus had a different influence on the differentiation between high- and low-ranking buildings in patients with and without HS.

Indeed, in patients with HS a separate ANOVA revealed a significant influence of the within-subjects factor STIMULUS ($F[1,17] = 14.02$; $p < 0.005$) but no other effects and no interaction with the side of epileptogenic focus. By contrast, in patients without HS we found both a significant effect of the factor STIMULUS ($F[1,8] = 15.62$; $p < 0.005$) and a significant interaction between STIMULUS and FOCUS ($F[1,8] = 11.85$; $p < 0.01$). In summary, the side of the epileptogenic zone influenced the differentiation between high- and low-ranking buildings in TLE patients without but not in patients with HS. Consequently, we collapsed ENPs of patients with right and left HS for the following comparisons with normal controls. However, since the side of the epileptogenic focus did matter in TLE patients without HS we could not collapse ENP data of these 4 patients with a left-sided and 6 patients with a right-sided lateralization of the epileptogenic focus and dispensed with statistical analyses in these two small patient groups.

To analyze the influence of TLE with HS on the processing of architectural stimuli we subjected mean amplitudes of HS+ patients to a repeated-measures ANOVA as described above–now, however, with the between-subjects factor TLE (healthy subjects vs. HS+). We found a significant influence of the factor STIMULUS ($F[1,31] = 41.88$; $p < 0.0005$) but no main effect of the between-subjects factor TLE ($F[1,31] = 3.93$; $p = 0.06$) There was, however, a significant interaction between these two factors ($F[1,31] = 5.37$; $p < 0.05$), indicating that the presence of TLE with HS influenced the differentiation between high- and low-ranking buildings in the ENP time-window (see Figure 9). Note, however, that our data cannot adjudicate between

the hypotheses that either HS or TLE is responsible for this influence on ENPs because we could not compare ENPs in patients with and without HS. Nevertheless, repeated-measures ANOVAs calculated separately for both groups revealed that in this time-window ERP responses of both healthy controls ($F[1,13] = 24.05$; $p < 0.0005$) and HS+ patients ($F[1,18] = 14.22$; $p < 0.005$) differentiated between the two classes of buildings. Post-hoc *t* tests for paired samples with Bonferroni correction showed that in healthy subjects, responses to low-ranking buildings from all 6 recordings sites were significantly higher in amplitude than those to high-ranking buildings ($p < 0.005$ at F3, F4, F7, F8, C3, and C4). In HS+ patients, however, these differences reached significance only at the frontal contacts F3 (low vs. high: 0.4 ± 4.3 µV vs. 1.4 ± 4.0 µV; $p < 0.05$) and F4 (1.3 ± 5.0 µV vs. 2.4 ± 4.5 µV; $p < 0.005$). Inspection of the grand averages of ENPs to both types of stimuli suggests that the differences between both responses were somewhat larger at all contacts in healthy controls. However, a MANOVA on mean amplitudes of the difference waves from the 6 recording sites showed no significant effect of the between-subjects factor TLE (healthy subjects vs. HS+; $F[6,26] = 2.44$; $p = 0.053$).

Late positive potentials (LPPs) in the 400–600 ms time-window

All classes of stimuli elicited late positive potentials (LPPs) peaking around 450 ms after stimulus presentation over central and parietal electrode contacts. We started our analyses of these potentials again by testing whether there were significant differences between patients with left- and right-sided TLE with and without HS. To this aim we calculated a repeated-measures ANOVA with mean amplitudes of LPPs to high- and low-ranking buildings with the between-subjects factors STIMULUS (high- vs. low-ranking buildings), SITE (central vs. parietal), and HEMISPHERE (left vs. right) as well as the between-subjects factors FOCUS (LTE vs. RTE) and HS

(HS+ vs. HS–). Here, we found a significant effect of the within-subjects factor STIMULUS ($F[1,25] = 17.40$; $p < 0.0005$) while effects of both between-subjects factors FOCUS and HS were not significant. There was, however, a significant interaction between STIMULUS and HS ($F[1,25] = 6.00$; $p < 0.05$) but not between STIMULUS and FOCUS ($F[1,25] = 0.46$; $p = 0.54$) indicating that HS but not the side of the epileptogenic focus influenced the differentiation between high- and low-ranking buildings by LPPs. Indeed, in two additional ANOVAS testing the influence of the side of the epileptogenic focus in patients with and without HS separately, we found no significant effects of the between-subjects factor FOCUS (HS+: $F[1,17] = 1.59$; $p = 0.22$; HS–: $F[1,8] = 1.16$; $p = 0.31$). Therefore, we collapsed LPP data of LTE and RTE patients in both the HS+ and the HS– group for the comparisons with healthy controls.

To analyze the influence of HS on LPPs elicited by architectural stimuli we again considered the stimulus types of high- and low-ranking buildings and calculated a repeated-measures ANOVA as described above–now with the between-subjects factor PATHOLOGY (healthy subjects vs. HS+ vs. HS–). Here, we found a significant influence of the factor STIMULUS ($F[1,40] = 51.89$; $p < 0.0005$) but no main effect of the between-subjects factor PATHOLOGY ($F[2,40] = 1.11$; $p = 0.34$). There was, however, a significant interaction between these two factors ($F[2,40] = 10.36$; $p < 0.0005$) indicating that pathology influenced the differentiation of the two classes of buildings by LPPs.

A separate ANOVA comparing patients with hippocampal sclerosis with healthy controls showed a significant influence of the factor STIMULUS ($F[1,31] = 48.80$; $p < 0.0005$) and a significant interaction between STIMULUS and the between-subjects factor TLE (healthy subjects vs. HS+; $F[1,31] = 24.56$; $p < 0.0005$) confirming that the presence of HS influenced the differentiation between high- and

low-ranking buildings by LPPs. Consequently, repeated-measures ANOVAs calculated separately for both groups showed that only LPPs of healthy subjects ($F[1,13] = 41.25$; $p < 0.0005$) but not of HS+ patients ($F[1,18] = 3.81$; $p = 0.07$) differentiated between both classes of buildings (see Figure 9). Post-hoc *t* tests for paired samples with Bonferroni correction showed that in healthy subjects LPPs to high-ranking buildings from all 4 recordings sites were significantly higher in amplitude than LPPs to low-ranking buildings ($p < 0.0005$ at C3, P3, P4; $p < 0.005$ at C4). By contrast, in HS+ patients there seemed to be a difference only at C3 (low vs. high: 0.0 ± 3.1 µV vs. 0.7 ± 3.3 µV; $p < 0.05$). However, this difference was not significant after Bonferroni correction. *T* tests for independent samples calculated for mean amplitudes of the difference-waves (LPPs to low- minus LPPs to high-ranking buildings) in both groups showed that control subjects had significantly larger difference waves than HS+ patients at C3, C4, P3, and P4 ($p < 0.005$ at all sites after Bonferroni correction) (see Figure 10).

By contrast, an ANOVA comparing healthy subjects with TLE patients without HS demonstrated significant effects of the within-subjects factor STIMULUS ($F[1,22] = 40.13$; $p < 0.0005$) but no effect of TLE (healthy subjects vs. HS–; $F[1,22] = 0.02$; n.s) and no interaction between both factors ($F[1,22] = 2.46$; n.s). Thus, the presence of TLE without hippocampal sclerosis did not compromise the differentiation between both building classes by LPPs (see Figure 11). The results of two additional analyses were concordant with these findings: within the group of TLE patients the between-subject factor HS (HS+ vs. HS–) had no significant effect on LPPs ($F[1,27] = 1.72$; $p = 0.2$). However, there was a significant interaction between HS and the within-subjects factor STIMULUS ($F[1,27] = 5.18$; $p < 0.05$). Calculating the same ANOVA for both groups separately, we found that the factor STIMULUS remained significant only for HS– patients ($F[1,9] = 8.60$; $p < 0.05$) but not for HS+ patients ($F[1,18] = 3.81$; $p = 0.07$).

In summary, we found that in patients with unilateral hippocampal sclerosis the normal differentiation between high- and low-ranking buildings was reduced within the 200–400 ms but abolished within the 400–600 ms time-window. Moreover, we found that in patients with TLE it is specifically hippocampal sclerosis that compromises the differential late positive response to high- and low-ranking buildings.

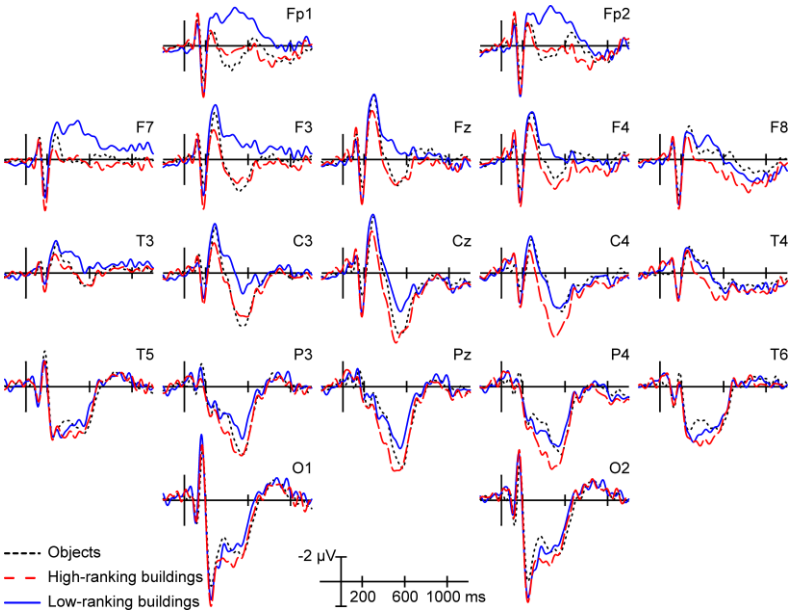

Figure 8. Grand average ERPs to objects (dotted black line), high- (dashed red line), and low-ranking (solid blue line) buildings at all electrode contacts in 14 healthy subjects. ERPs are plotted between -200 and 1200 ms and re-referenced to linked mastoids. The ENP (early negative potential) at frontal electrode site (e.g. F3/F4) as well as the LPC (late positive component) at parietal sites (e.g., P3/P4) differentiate between high- and low-ranking buildings.

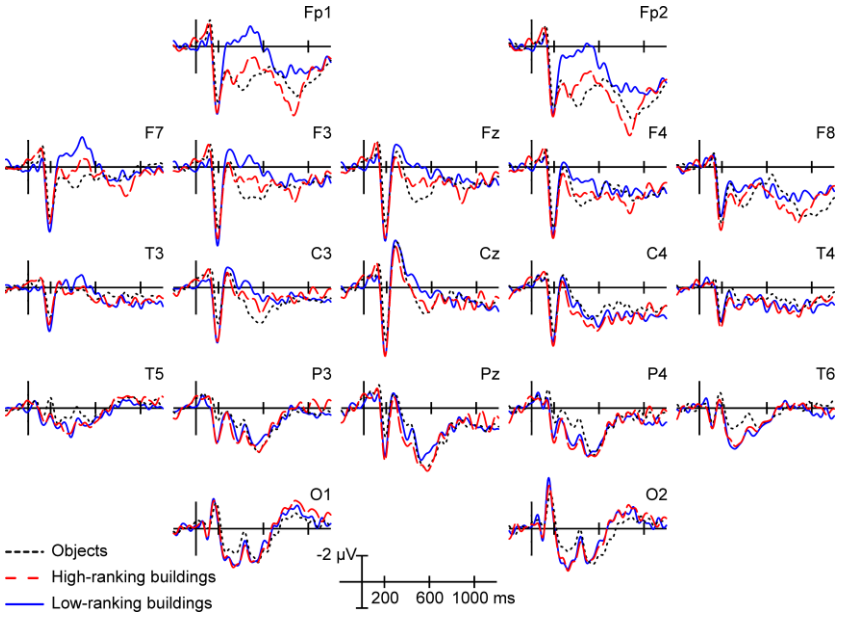

Figure 9. Grand average ERPs to objects (dotted black line), high- (dashed red line), and low-ranking (solid blue line) buildings at all electrode contacts in 20 patients with temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS). ERPs are plotted between -200 and 1200 ms and re-referenced to linked mastoids. Note that the presence of HS in TLE patients affects the differentiation between high- and low-ranking buildings in the LPC (late positive component) at parietal sites (e.g. P3/P4).

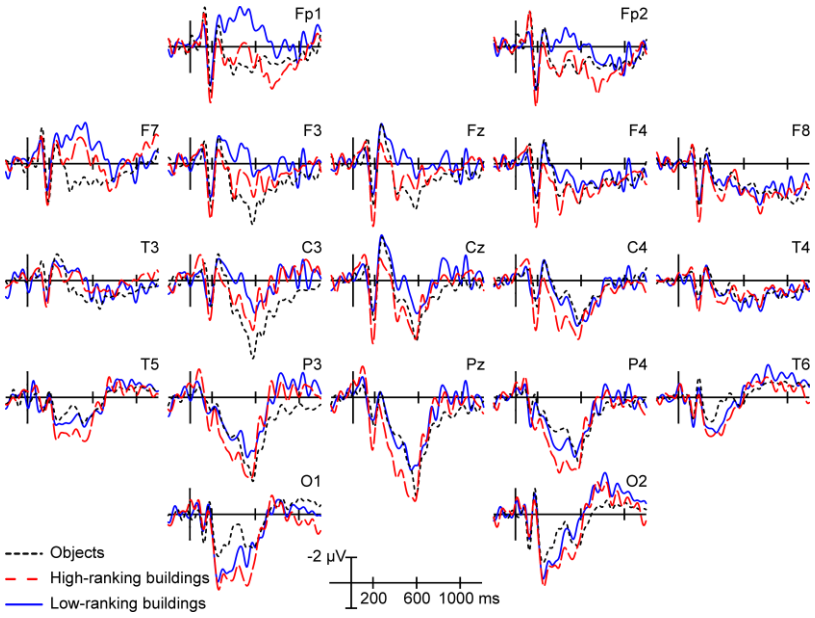

Figure 10. Grand average ERPs to objects (dotted black line), high- (dashed red line), and low-ranking (solid blue line) buildings at all electrode contacts in 10 patients with temporal lobe epilepsy (TLE) without hippocampal pathology. ERPs are plotted between -200 and 1200 ms and re-referenced to linked mastoids. Note that the presence of HS in TLE patients affects the differentiation between high- and low-ranking buildings in the LPC (late positive component) at parietal sites (e.g. P3/P4).

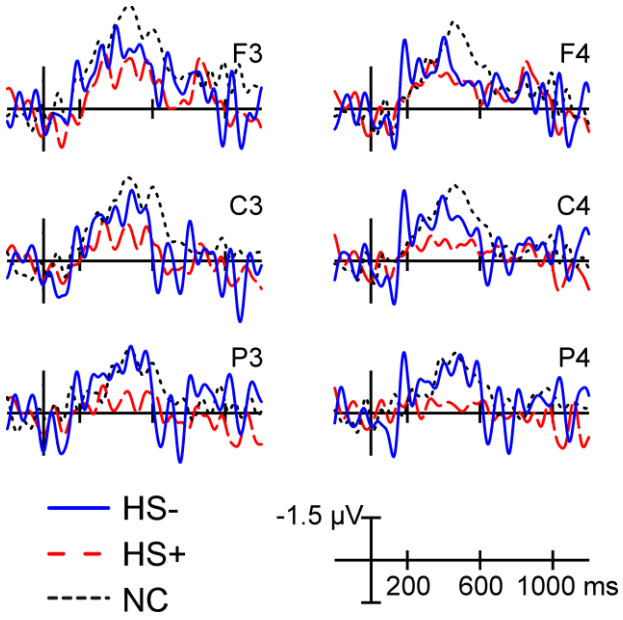

Figure 11. Difference waves for healthy subjects (dotted black line), TLE patients with (dashed red line) and TLE patients without (solid blue line) hippocampal sclerosis (HS). Difference waves were computed by subtracting responses to high-ranking from those to low-ranking buildings for each group separately.

Additional observations

Prominent in occipital recordings is a negative component peaking around 250 ms (N250). To test whether these potentials of high- and low-ranking buildings were different in patients with left- and right-sided TLE with and without HS we submitted their peak amplitudes of the occipital electrodes O1 and O2 to a repeated-measures ANOVA with the within-subjects factors STIMULUS (high- vs. low-ranking buildings) and HEMISPHERE (left (O1) vs. right (O2)) and the between-subjects factors FOCUS (left vs. right) and HS (HS+ vs. HS–). While no factor had a significant effect, there was a significant interaction between the between-subjects factors FOCUS and HS. Separate ANOVAs for both patient groups revealed that the side of the epileptogenic focus had no influence in HS+ patients ($F[1,17] = 1.54$; $p = 0.23$), but it had a significant effect in HS– patients ($F[1,27] = 5.95$; $p < 0.05$). In this group patients with right-sided TLE had lower N250 responses over the right occipital lobe than patients with left-sided TLE to both high-ranking (3.9 ± 4.8 µV vs. 11.2 ± 2.2 µV;

$p < 0.5$) and low-ranking buildings (3.6 ± 4.7 µV vs. 10.7 ± 2.2 µV; $p < 0.5$) although these effects were not significant after Bonferroni correction. Consequently, N250 data of LTE and RTE patients with HS could be collapsed while this was not possible for HS– patients.

An additional ANOVA comparing HS+ patients with normal controls revealed a significant effect of the between-subjects factor TLE (healthy subjects vs. HS+; $F[1,31] = 8.76$; $p < 0.01$). Post-hoc *t* tests confirmed that on both sides N250 amplitudes to both high- and low-ranking buildings were significantly smaller in amplitude in TLE patients with HS than in healthy subjects: O1 (high-ranking): 4.8 ± 4.4 µV vs. 10.7 ± 7.8 µV ($p < 0.05$); O2 (high-ranking): 5.0 ± 5.2 µV vs. 10.3 ± 6.2 µV ($p < 0.05$); O1 (low-ranking): 4.4 ± 4.1 µV vs. 10.5 ± 7.4 µV ($p < 0.01$); O2 (low-ranking): 4.5 ± 5.1 µV vs. 10.5 ± 6.3 µV ($p < 0.0005$). However, only the difference of responses to low-ranking buildings remained significant after Bonferroni correction.

DISCUSSION

To examine whether the hippocampus participates in the differentiation between high- and low-ranking buildings and whether hippocampal sclerosis interferes with this process we recorded event-related potentials (ERPs) in healthy subjects and in patients with temporal lobe epilepsy (TLE) with (HS+) and without (HS–) hippocampal sclerosis. In line with results from our previous study performed in a different group of healthy subjects (Oppenheim et al., 2009) we could show that ERP responses normally differentiate between high- and low-ranking architectural stimuli that are ranked according to the rhetorical theory of decorum. Here, we found that between 200 and 400 ms this differentiation was reduced but still significant in both

HS+ and HS– patients–independent of its side. By contrast, the normal differentiation between both classes of buildings between 400 and 600 ms was completely abolished in both patients with left- and patients with right-sided hippocampal sclerosis. Thus, our findings show for the first time that the hippocampus contributes to the visual processing of architectural ranking and that late positive potentials differentiate between TLE patients with and without hippocampal sclerosis.

Occipital responses and performance

The finding that occipital N250 potentials to both high- and low-ranking buildings were significantly reduced in amplitude in HS+ patients was neither expected nor within the scope of our present study. Therefore, we can only speculate on possible reasons for this finding. First, we did not carry out formal measurements of the visual acuity of our participants. Consequently, we cannot exclude the possibility that differences in this parameter may have influenced early occipital responses. Second, of course, it cannot be excluded that the antiepileptic medication may influence ERPs in TLE patients, although data especially on more modern drugs are scarce. On the other hand, TLE itself may play a role because it has been shown that TLE patients exhibit reduced N270 amplitudes to faces (Sun et al., 2008) and to not memorized stimuli (Sun et al., 2007). In addition, visual evoked posterior N200 potentials in patients with partial seizures were found to be particularly affected by the presence of a temporal epileptogenic focus (Verleger et al., 1997). Future studies will have to address the question of whether the reduction of N250 amplitudes is confined to HS+ patients, thus perhaps indicating hippocampal influences on occipital visual processes, or whether this effect can also be found in other epilepsy patients and may even be related to medical treatment. However, to our knowledge, no deficits in early visual processes have yet been reported in TLE patients

(Grant et al., 2008). Therefore, it could also be speculated that reduced attention may have contributed to diminished N250 amplitudes and reduced categorization performance in our TLE patients. Nevertheless, the fact that our patients classified more than 90% of all buildings and objects correctly indicates that they were able to perform the experimental task. Moreover, neither effects of the antiepileptic medication nor reduced attention could explain the observed differential effect of hippocampal sclerosis on ENPs and LPPs.

Finally, a more detailed examination of the low-level visual characteristics of the two groups of stimuli and, in particular, of their spatial frequency structure, may provide additional and important contributions to understand ERP correlates of visual processing of low- and high-ranking buildings in TLE patients. For example, recent evidence suggests that the beta and gamma values underlying the contrast distribution of an image, can explain up to 70% of the variance of early ERP responses to visual stimuli (Scholte et al., 2009).

Fronto-central ENPs between 200 and 400 ms

N350 potentials recorded from the scalp have been shown to be associated with visual object model selection and the processing of visual objects in perceptual representation systems (Schendan and Kutas, 2002, 2003). In addition, the sensitivity of the N350 to repetition implicates this ERP component in implicit memory without conscious awareness based on visual perceptual (Schendan and Kutas, 2007; Schendan and Maher, 2009) or conceptual processes (Voss and Paller, 2006; Holcomb and McPherson, 1994). On the other hand, N350 repetition effects may also index familiarity based on episodic explicit memory with awareness (Curran et al., 2002; Duarte et al., 2004). The latency of the N350 may partially overlap with

that of the N400, a potential that is sensitive to a variety of factors including word frequency and class, semantic expectancy, repetition, concreteness etc. (Kutas and Van Petten, 1994) and may also reflect conceptual implicit memory (Rugg, et al., 1998). Other memory related ERP paradigms have identified an FN400 or "mid-frontal old/new effect" at frontal and fronto-central recording sites, which is characterized by more positive going waveforms for repeated as compared to new items between 300 and 500 ms independent of conscious recollection, thus implicating the FN400 with familiarity memory processes (for a review see Mecklinger, 2006). In earlier studies with intrahippocampal depth electrodes some members of our group identified a negative ERP component that was generated within the hippocampus proper, peaked around 300 ms after stimulus presentation and was higher in amplitude to unidentified as compared to identified visual objects (Vannucci et al., 2006). In addition, a negative component peaking around 350 ms was larger to nonsense than to real objects (Vannucci et al., 2003). However, the relation of these potentials to those recorded from the scalp is not clear. Intracranial recordings have also identified N400 potentials in temporal, frontal and parietal regions, thus indicating that surface N400s may represent the summation of a variety of different mechanisms (e.g. Guillem et al., 1995a).

In this study, we found that the differentiation between high- and low-ranking buildings by ENPs peaking around 330 ms was somewhat reduced in HS+ patients as compared to healthy control subjects. However, because we could not collapse ENP data of LTE and RTE patients without HS, we could not compare HS– patients to HS+ patients and normal controls. Therefore, we cannot prove whether the difference between HS+ patients and normal controls was caused by hippocampal sclerosis or by temporal lobe epilepsy as such. However, this difference was *quantitative* not *qualitative* in nature, because ENPs differentiated significantly between high- and low-ranking buildings in both groups of subjects.

This lack of a more pronounced effect of HS on ENPs elicited by pictures of buildings is consistent with findings from intracranial recordings of N400 potentials to visual stimuli: Elger et al. (1997) found N400 potentials elicited by words and pictures in both lateral and medial temporal regions. Those to pictures, however, were not influenced by TLE, a result that has also been found by several other studies (Puce et al., 1991; Guillem et al., 1995a; Dietl et al., 2008). By contrast, N400s recorded not only with depth electrodes within the medial temporal lobes (Grunwald et al., 1995, 1998) but also from scalp electrodes (Smith and Halgren, 1989; Rugg et al., 1991; Lalouschek et al., 1998; Olichney et al., 2002) have shown that N400s to words may well be reduced in amplitude by the epileptogenic process. On the other hand, because of its latency and scalp distribution the ENP reported here resembles the N350 more closely than the scalp-N400. However, to our knowledge, N350 potentials in visual categorization tasks have not yet been recorded from the scalp in epilepsy patients, so that we cannot compare our findings with earlier results.

For identification and categorization a visually perceived object must reactivate abstract knowledge in a semantic memory network, which eventually makes naming possible (Martin, 2007). Initially, an object model has to be selected from long-term memory that fits the visual structure of the perceived object as good as possible (Schendan and Kutas, 2002). Associated with this process of object model selection are negative ERP components peaking around 350 and 390 ms, i.e. within the time-window from 200–400 ms, at fronto-polar and fronto-central sites (Schendan and Kutas, 2002, 2003, 2007a). In particular, the fronto-central N390 is larger for incongruent than congruent objects in the context of a scene (e.g. a desk in a river vs. a pot in a kitchen), thus resembling the sensitivity of the N400 to semantic incongruity (Ganis and Kutas, 2003). From the perspective of this line of research, our finding of more negative going ENPs to low- than to high-ranking buildings suggests that it may be easier to find matching object models for high-ranking

buildings. That this process relies on the interaction of occipital and frontal areas and depends more on conceptual implicit memory processes presumably in anteromedial temporal areas than on explicit memory processes that are mediated by the hippocampus, may explain why HS does not abolish the differentiation between both classes of architecture during the 200–400 ms time-window. Independent of HS, however, TLE interferes with this differentiation to some degree (without preventing it). This finding is consistent with MEG results showing that the temporal lobe contributes to object categorization in a time-window from 210 to 450 ms (Löw et al., 2003). Therefore, we take our findings to suggest that visual processing of buildings based on the architectural decorum entails object model selection and implicit memory processes that are mediated–at least in part–by temporal lobe structures but not the hippocampus proper.

Centro-parietal LPPs between 400 and 600 ms

LPCs recorded from the scalp have been shown to be associated with secondary object categorization and explicit recollection processes (Schendan and Kutas, 2002; Schendan and Maher, 2009). Other studies have shown that the LPC and P600 potentials peaking in a similar time-window are sensitive, e.g., to word frequency and repetition (Rugg et al., 1995; Rüsseler et al., 1995), lexicality (Curran 1999), and linguistic–especially syntactic–incongruities (e.g., Friederici et al., 1999; Osterhout et al., 2002; Hagoort, 2003).

Memory-related paradigms have associated this late ERP response specifically with recollection instead of familiarity memory (e.g. Paller and Kutas, 1992; Wilding et al., 1995; Düzel et al., 1997). Intracranial recordings have identified late positive (or P600) potentials generated within the (non-epileptic) hippocampus proper to words

(e.g. Guillem et al., 1995b; Grunwald et al., 2003), to pictures of real but not nonsense objects (Vannucci et al., 2003), to identified but not unidentified objects (Vannucci et al., 2006), to famous faces (Trautner et al., 2004; Dietl et al., 2005), and to words with high imageability (Klaver et al., 2005).

Here, we found that LPPs peaking around 450 ms differentiated reliably between high- and low-ranking buildings in healthy subjects and in TLE patients without HS while this differentiation was completely absent in HS+ patients. This significant effect of HS on LPPs is consistent with findings from intrahippocampal depth recordings which showed that the normal hippocampal differentiation between real and nonsense objects by a late positive component is absent in sclerotic hippocampi (Vannucci et al., 2003). In scalp recordings, P600 potentials and LPCs have been found to show reduced sensitivity to word repetition in patients with left but not right TLE (Olichney et al., 2002) and in patients with mild Alzheimer's disease (Olichney et al., 2006; for a review see Taylor and Olichney, 2007). However, to our knowledge, scalp P600s to visual stimuli have not been studied yet in TLE patients.

After object model selection the successful identification of visual objects calls upon a later processing sequence during which secondary categorization-related processes take place (Schendan and Kutas, 2002) that are associated with the generation of an LPC. This component has been linked not only to categorization but also to stimulus evaluation processes (McCarthy and Donchin, 1981), the activation of semantic knowledge and naming (Damasio et al., 1996), and incidental (Schendan and Kutas, 2003) and possibly conscious recollection (Paller et al., 1995; Duarte et al., 2004). Our finding of more positive going LPPs to high- than to low-ranking buildings in subjects without HS may thus indicate that high-ranking buildings elicit more semantic knowledge and/or more explicit memory processes than low-ranking buildings. Hippocampal sclerosis, however, eliminates the

sensitivity of the LPP to architectural ranking. Therefore, we take our results to suggest that the hippocampus proper contributes to secondary visual categorization processes of buildings based on the architectural decorum. The effect of HS on LPPs had no influence on response times or accuracy of responses. However, future studies may examine whether episodic and semantic memory processing of architectural stimuli may be affected in TLE patients with hippocampal sclerosis.

CONCLUSIONS

Theories of rhetoric and architectural design have postulated since a long time that buildings have more or less impact on the minds of their beholders according to a ranking of architectural ornaments between the two poles of the "sublime" and the "low." However, to our knowledge, this assumption has not been tested scientifically yet with neurophysiological methods. Our findings indicate that visual processing as indexed by two different ERP components is indeed sensitive to the architectural decorum: an early negative potential (possibly an N350) differentiated reliably between high- and low-ranking buildings in healthy subjects and in TLE patients with and without hippocampal sclerosis. By contrast, a late positive potential (possibly an LPC or P600) differentiated between both classes of buildings only in healthy subjects and in TLE patients without hippocampal pathology while it did not in patients with hippocampal sclerosis. Thus, we found that the hippocampus proper does indeed contribute critically to architectural ranking inference and that this process is compromised in medial temporal lobe epilepsy with hippocampal sclerosis. However, our findings cannot adjudicate the question of whether hippocampal contributions to the visual processing of buildings are more related to episodic memory processes or the semantic processing of visual stimuli: high-ranking buildings could elicit prototypical (or for that matter "false") memories

by alluring recollections of sublime buildings from episodic memory and/or they could be easier to verbalize. Future studies may want to address this question.

ACKNOWLEDGMENTS

We thank Peter Hilfiker and Ian Mothersill for technical support and Gerhard Blechinger for helpful suggestions. We also would like to thank two anonymous reviewers for their valuable comments regarding the improvement of our manuscript.

DISCLOSURE

Ilan Oppenheim has designed and created the experiment, recruited and informed all participants, obtained ERP data, carried out ERP post-processing and statistical analysis, and written the draft and the manuscript of this article.

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A3) Encoding and recognition of architectural ranking

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Key words:

Event-related potentials, recognition memory, visual processing, study and test, architecture, decorum

ABSTRACT

Since the ancient world architecture generally distinguishes two categories of buildings with either high- or low-ranking design. We recently could show that event-related potentials (ERPs) to pictures of high-ranking buildings are significantly more positive in amplitude than ERPs elicited by low-ranking buildings in a time window of 300–600 ms after stimulus presentation. To address the question of whether memory processes may be associated with these brain electrical responses we now performed a recognition experiment using a study-test-design. Replicating our previous findings we found that responses between 300–500 ms distinguished reliably between high- and low-ranking buildings during both study and test. In addition, both N400s and late positive components (LPCs) were more positive in amplitude to repeated than to new pictures of buildings. By contrast, while both classes of stimuli elicited a late positive component (LPC) that was sensitive to recognition, only high- but not low-ranking buildings elicited pronounced LPCs even during study. We take our data to suggest, that pictures of high-ranking but not low-ranking buildings can elicit memory processes associated with both familiarity and recollection even when they are perceived for the first time.

5 GENERAL DISCUSSION

A major focus of the present study lay in the investigation of visual object processing of buildings designed according to the classical decorum. This theory of rhetoric and architectural design postulates that architectural ornaments mark buildings as either high- or low-ranking so that these buildings have either more or less impact on the minds of their beholders. According to this theory, high-ranking architectural designs are thought to make buildings more prominent and thus more memorable and eventually more familiar, at least to subjects born and raised in Western culture. In a series of three experimental studies investigating healthy subjects and patients with temporal lobe epilepsy (TLE) we set out to test this assumption by recording ERPs to drawings of fictitious buildings with either high- or low-ranking architectural ornaments.

Results of these studies show that electrical brain responses do indeed differentiate between high- and low-ranking buildings by more positive going amplitudes to high-ranking buildings in an N400 time window for both healthy subjects and patients with TLE both with and without hippocampal sclerosis (HS). In contrast, late positive potentials were higher in amplitude to high-ranking buildings only in healthy subjects and TLE patients without, but not in TLE patients with HS.

Thus, we were able to show for the first time that the human hippocampus proper does indeed contribute critically to architectural ranking inference and that this process is compromised in medial TLE with HS. More generally, our findings suggest that the differentiation between high- and low-ranking buildings entails both early visual object selection and late post-model selection processes and that the hippocampus proper contributes critically to this second stage of visual object categorization. Furthermore, we suggest our findings indicate that architectural ornaments traditionally judged as high-ranking indeed elicit a greater sense of familiarity than low-ranking ornamental modules.

5.1 First study: Brain electrical responses to high- and low-ranking buildings

Results from our pilot study revealed that brain electrical responses differentiate reliably between high- and low-ranking stimuli. In a follow-up experiment that used a different sample of healthy subjects, we were able to replicate our previous findings with confirmatory data demonstrating brain amplitudes 300–500 ms after stimulus presentation (N400) over frontal electrodes that were more negative for low- as compared to high-ranking buildings for both healthy subjects and patients with TLE.

N400

ERP studies investigating visual processing of buildings are scarce. In fact, previous ERP experiments in this area of research mostly focused on brain activations elicited by buildings as such but not on brain regions or processes differentiating between different kinds of buildings (Iidaka et al., 2000; Engst et al., 2006). We take our finding that ERP responses to these stimuli show maximal differences in the N400 time window to suggest that the differentiation between high- and low-ranking buildings may be influenced by memory processes.

Numerous studies of ERP responses to visual and verbal stimuli indicate increased N400 components to be sensitive to familiarity, (e.g. Mecklinger, 2006; Curran & Hancock, 2007). They may thus also reflect implicit memory processes independent of conscious recollection (Rugg 1998; Rugg & Curran, 2007). For example, in "old vs. new" recognition paradigms, N400 potentials have been found to be reduced to stimuli that are judged as "old", even when subjects cannot recollect specific details from the study episode (Curran & Hancock, 2007). This well-known mid-frontal effect is characterized by reduced N400 amplitudes especially over frontal electrodes (e.g. Düzel et al., 2001; for a review see Mecklinger, 2006). With regards to the architectural decorum, it seems likely that buildings distinguished by high-ranking ornamental modules create more lasting memories, eventually leaving an impression of familiarity. Concordant with this hypothesis, we found that ERP responses elicited by high-ranking buildings were smaller in amplitude compared to those elicited by low-ranking buildings, thus, indicating a possible familiarity effect for the former.

Semantic aspects

Our drawings of buildings were artificially designed and did not depict existing architecture. As a consequence, if the processing of high-ranking buildings tapped indeed into familiarity, the associated memories cannot have been episodic but may, perhaps, refer to "prototypes" of buildings characterized by specific high-ranking ornaments. Following this hypothesis it can also be asked whether "prototypical" high-ranking buildings are easier to verbalize. In fact, in addition to reflect stimulus familiarity, increased brain amplitudes in this time window have been associated with semantic expectancy, repetition, and concreteness (Kutas and Van Petten, 1994). Accordingly, the N400 is smaller in response to high frequency words (Meyer et al., 2006) and attenuated by semantic priming (e.g. Nobre and McGarthy, 1994), or conceptual processing (Voss and Paller, 2009). It is suggested that expected or familiar stimuli require less effort to activate pre-existing semantic network, resulting in decreased N400 components (Kutas, 1998, 2000).

For identification and categorization of a visually perceived object, abstract knowledge in a semantic memory network must be reactivated eventually to provide adequate naming (Martin, 2007). In this respect, studies have revealed a fronto-central N390 that is larger in response to incongruent than to congruent objects in the context of a scene, thus, resembling the sensitivity of the N400 to semantic incongruity (Ganis and Kutas, 2003). Therefore, semantic processing may have been triggered more easily by prototypical ornaments that we used to depict high-ranking buildings than by those marking low-ranking architectural designs (i.e. "mosque", "temple", "church" vs. "house"). This semantic (and therefore “elaborate") processing may also make high-ranking buildings easier to encode. Our finding of less negative going ENPs to high- than to low-ranking buildings may thus indicate lesser efforts needed in order to find matching object models for high-ranking buildings.

Additional support for this hypothesis is the observance that ERPs of high-ranking buildings are also much more similar to ERPs elicited by the everyday life objects that represent stimuli with easy access to the semantic network (see Figure 5)**}**. Based on our findings of decreased N400 potentials for high-ranking buildings we cannot exclude that the perception of stimuli that are distinguished by high-ranking ornamental modules provides facilitated access to or retrieval from the semantic network.

Reports from intracortical ERP studies using intrahippocampal depth electrodes support our hypothesis. In general, more positive-going ERP responses have been recorded from within the hippocampus proper for verbalizable pictures (Vannucci et al., 2006). More specifically, two negative components peaking at 300 and 350 ms were higher in amplitude to unidentified as compared to identified visual objects (Vannucci et al., 2006), and larger to nonsense than to real objects (Vannucci et al., 2003). Although these findings are in line with our hypothesis, the relation of these potentials to those recorded from the scalp is not clear since the hippocampus is, at least in part, an electrically closed field (Klee and Rall, 1977) and ERPs generated within the hippocampus are attenuated in extrahippocampal recordings (Grunwald et al., 1999). Nevertheless, our data of smaller N400 potentials for high-ranking buildings coincide with findings from intrahippocampal and surface ERP studies showing more positive brain responses to verbalizable objects, thus suggesting semantic aspects to be involved in the processing of high- and low-ranking buildings. Independent of the precise nature of the underlying neuropsychological processes, however, our findings indicate that the hippocampal formation participates in the perception ranking of visual stimuli according to the architectural decorum.

Object identification model

A first step of visual object identification has been described as visual object model selection (Schendan and Kutas, 2002, 2003). As proposed by Schendan and Kutas (2002), this object model selection process reflects implicit categorization knowledge with access to semantic and perceptual long-term memory that fits the visual structure of the stimulus (Schendan & Kutas 2002, 2003; Nobre and McGarthy, 1994). Associated with this process of object model selection during stimulus integration are negative ERP components peaking around 350 and 390 ms (N350) at fronto-polar and fronto-central sites (Schendan and Kutas, 2002, 2003, 2007a). The N350 is modified by perceptual and conceptual implicit memory processes (Schendan and Kutas, 2003, 2007a, Schendan and Maher, 2009) and by perceptual expertise (Schendan and Kutas, 2003). In fact, these studies indicate that the fronto-central N350 seems to be a complex of distinct ERP subcomponents reflecting the hierarchical activation of different but interacting "perceptual" knowledge that is specifically related to the visual structure of the object and more abstract and conceptual kinds of object knowledge.

The most prominent ERP component associated with visual object processing is an N350 component, a subcomponent of the frontal N400, that is proposed to reflect an early search through an object selection system. The N350 is sensitive to visual perceptual (Schendan and Kutas, 2007; Schendan and Maher, 2009) or conceptual processes (Voss and Paller, 2006; Holcomb and McPherson, 1994). Similar to the N400 component discussed above, N350 amplitudes have been shown to be sensitive to repetition, thus, implicating this ERP component also in implicit memory without conscious recollection (Schendan and Kutas, 2007). This effect is assumed to arise from the attenuation of a frontally focused N400-like component presumably reflecting the facilitated access to conceptual and perceptual information related to the test item (Mecklinger, 2006, Curran, 1999). Notably, the latency of the N350 may partially overlap with that of the N400. Since we were interested in neurophysiological correlates of the processing of architectural ranking and did not specifically probe pre-existing data we cannot simply presuppose that the ERP amplitudes recorded in our studies are identical with an N350 or N400 component described in literature. Furthermore, since intracranial recordings suggest that several generators in multiple brain regions can contribute to a common scalp ERP component, surface ERPs may represent the summation of a variety of different mechanisms (e.g. Guillem et al., 1995a). Consequently, we cannot simply impute our findings of increased negative amplitudes in this time window to either the N350 or the N400 component since both share common characteristics such as time of onset, cortical distribution, and functional significance, i.e. reflection of conceptual implicit memory (Rugg, et al., 1998; Schendan and Kutas, 2007).

Novelty

On the other hand, increased N400 amplitudes have been related to novelty detection (Grunwald et al., 1998). Therefore it could be hypothesized that the enhanced frontal negativity elicited by low-ranking buildings may indicate greater novelty. However, since low-ranking buildings typically represent "normal", "everyday" buildings associated with economy or the private life, it is hard to conceive how these stimuli should elicit specific novelty effects. Furthermore, ERPs elicited by low-ranking buildings lack a fronto-central positivity, which traditionally has been associated with novelty detection (e.g. Goldstein et al., 2002; Dien et al., 2003).

Symmetry and complexity

Taking into account that our stimuli were used for the first time in an electrophysiological experiment, alternative explanations for our findings have to be considered. Could, for example, other graphical features of the stimuli be responsible for the different ERP patterns? In particular, symmetry (Jacobsen & Hofel, 2003) and stimulus complexity (Eisenman, 1968; Berlyne, 1970) have been found to influence aesthetic judgments of beauty. However, all our stimuli were designed for the purpose of the experiments taking particular care to be matched for comparable size, contrast, complexity and symmetry between the two buildings categories.

Since it was the nature (i.e. Doric vs. Corinthian columns etc.) but not number of ornaments that differentiated our sets of high- and low-ranking stimuli, it could be argued that low-ranking buildings may have been perceived as less beautiful on other grounds than those of complexity and symmetry. In this respect, graphic patterns that were judged as not beautiful were found to elicit increased N400-like ERP responses compared to patterns judged as beautiful (Jacobsen and Höfel, 2003). The scalp topography of this negative deflection to non-beautiful stimuli suggested an involvement of the frontal cortex–a hypothesis also supported by fMRI-data (Jacobsen et al., 2006). Although our data of increased N400 amplitudes for low- compared to high-ranking buildings seem to be concordant with these findings, the chosen strategy of our experiments did not ask our subjects to make aesthetic judgments about the stimuli. Indeed, in a follow-up study that did not require an overt aesthetic judgment and, thus, is more comparable to our design, Höfel and Jacobsen (2007) were not able to replicate their findings of an early fronto-central negativity for less attractive patterns.

In sum, we take our findings of differentiating brain electrical responses to high- and low-ranking buildings to suggest that the perception of architectural design is sensitive to rules of the classical decorum system, at least in persons born and raised in Western cultures. In addition, we propose that high-ranking ornaments can help to facilitate the visual processing of buildings–either by making them semantically classifiable or by eliciting familiarity memory processes.

5.2 Second study: Hippocampal contribution to the processing of architectural ranking

Early negative potentials

Since both patients with and without HS show early negative potentials that differentiate between high- and low-ranking buildings in the N400 time window, our findings indicate that HS does not prevent the associated visual subprocesses. Although MEG results report that the temporal lobe contributes to object categorization in an early time window similar to the one in our study (Löw et al., 2003), we suggest that the differential processing of the two classes of architecture during the N400 time window relies more on occipito-frontal interactions and depends more on conceptual implicit than on explicit memory processes that are mediated by the hippocampus. However, the observation that TLE interferes with this differentiation to some degree (without preventing it) independent of HS suggests that visual processing of buildings based on the architectural decorum entails early object model selection and implicit memory processes that are mediated–at least in part–by temporal lobe structures but not the hippocampus proper.

Late positive potentials

As described above, object model selection involves the activation of associated knowledge that may support finding a name and recollecting earlier encounters with the perceived object. Following the initial identification of visual objects a later processing sequence is required during which secondary categorization-related processes take place (Schendan and Kutas, 2002). These post-model selection processes are associated with the generation of a parietal late positive component (LPC) that has been linked not only to categorization but also to stimulus evaluation processes (McCarthy and Donchin, 1981) and the activation of semantic knowledge and naming (Damasio et al., 1996).

Moreover, the LPC has also been shown to reflect incidental (Schendan and Kutas, 2003) and possibly conscious recollection (Voss and Paller, 2008, Paller et al., 2007; Rugg and Curran, 2007; Duarte et al., 2004; Friedman and Johnson, 2000; Mecklinger, 2000; Paller et al., 1995; Paller and Kutas, 1992). This top-down parsing of object identification has been proposed to reflect secondary categorization and

stimulus evaluation processes (Kutas 2007; Schendan & Kutas 2003; McCarthy and Donchin, 1981) and may also tap aspects of explicit episodic memory processes (Schendan and Kutas, 2007a; Schendan and Maher, 2009). Although several brain regions seem to contribute to LPC effects (Guillem et al., 1995), temporal regions have been directly linked to object knowledge naming (Damasio, 1996) and the activation of semantic knowledge (Kutas, 2002).

In our second study we found late positive potentials (LPPs) peaking around 450 ms that differentiated reliably between high- and low-ranking buildings in healthy subjects and in TLE patients without HS, whereas this differentiation was completely absent in HS+ patients. Thus, besides reflecting familiarity processes in an early N400 component, ERP results from the follow-up study suggest that the processing of high- and low-ranking buildings may in addition entail explicit recollection processes (Schendan and Kutas, 2002; Schendan and Maher, 2009) that are compromised in the presence of hippocampal damage.

Memory

Scalp recording ERP studies have shown that the LPC and P600 potentials are sensitive to word frequency and repetition (Rugg et al., 1995; Rüsseler et al., 1995), lexicality (Curran 1999) and linguistic incongruities (e.g., Friederici et al., 1999; Osterhout et al., 2002; Hagoort, 2003). Memory-related paradigms have associated this late ERP response specifically with recollection instead of familiarity memory (e.g. Paller and Kutas, 1992; Wilding et al., 1995; Düzel et al., 1997). Also, intracranial recordings have identified late positive (or P600) potentials generated within the (non-epileptic) hippocampus proper to words (e.g. Guillem et al., 1995b; Grunwald et al., 2003), to pictures of real but not nonsense objects (Vannucci et al., 2003), to identified but not unidentified objects (Vannucci et al., 2006), to famous faces (Trautner et al., 2004; Dietl et al., 2005), and to words with high imageability (Klaver et al., 2005).

Here, we found a late positive potential (possibly an LPC or P600) that differentiated between both classes of buildings only in healthy subjects and in TLE patients without hippocampal pathology but not in patients with hippocampal sclerosis.

This significant effect of HS on LPCs is consistent with findings from intrahippocampal depth recordings showing that the normal hippocampal differentiation between real and nonsense objects by a late positive component is absent in sclerotic hippocampi (Vannucci et al., 2003). Unfortunately, to our knowledge, scalp P600s to visual stimuli have not been studied yet in TLE patients, hence we are unable to compare our results properly.

Nevertheless, our findings of more positive going LPPs to high- than to low-ranking buildings in subjects without HS may indicate that high-ranking buildings elicit more semantic knowledge and/or more explicit memory processes than low-ranking buildings. Hippocampal sclerosis, however, eliminates the sensitivity of the LPP to architectural ranking. Therefore, we take our results to suggest that the hippocampus proper contributes to secondary visual categorization processes of buildings based on the architectural decorum. Demonstrating pronounced ERP differences in an early (N400) and a late (LPC) time window we furthermore take our data to suggest that both implicit and explicit memory processes are involved in the perception of visual objects that follow the architectural decorum.

6 SUMMARY AND CONCLUSION

The present thesis aimed to shed light on different aspects of the visual object processing of stimuli that are designed according to the classical decorum in healthy subjects and patients with temporal lobe epilepsy (TLE). A major finding of this work is the observation that scalp recorded ERPs reliably differentiate between pictures of high- and low-ranking buildings by showing more positive brain amplitudes for the former in an early (N400) and late (LPC or P600) time window. In line with reports from the literature, we interpret our data of increased positivity for high-ranking compared to low-ranking buildings in the early N400 time window to reflect implicit memory processes that provide facilitated access to pre-existing knowledge in the semantic network and long-tem memory. Supporting the assumptions of the rhetorical theory of architectural decorum, we therefore take our findings to suggest that high-ranking ornaments can help to facilitate visual processing of high-ranking buildings by making them more semantically classifiable or by eliciting familiarity memory processes.

Likewise, a late positive potential (possibly an LPC or P600) reflecting secondary categorization-related processes also demonstrated different ERP responses between high- and low-ranking buildings in healthy subjects and in TLE patients without hippocampal damage, independent of the epileptogenic focus. Conversely, while differentiating ERP responses in the early N400 were not affected in TLE patients, the differentiation was completely absent in TLE patients with either left- or right-sided hippocampal sclerosis. Thus, the studies reported in this thesis extend previous work on visual object processing by showing that the human hippocampus not only critically contributes to secondary visual categorization processes of stimuli based on the architectural decorum, but also essentially supports architectural ranking inference and that this process is compromised in medial TLE with hippocampal sclerosis. Thus, by demonstrating that the medial temporal lobes support the processing of high-ranking buildings and that the differentiation between stimuli of high- and low-ranking buildings is affected in the presence of hippocampal sclerosis our data contribute to the understanding of the hippocampal contribution to the processing of stimuli based on the architectural decorum.

In conclusion, we take our data to propose that the perception of high- and low-ranking buildings entails both early implicit and late explicit memory processes that support facilitated processing of high- compared to low-ranking buildings by providing facilitated access to semantic knowledge stored in long-term memory.

7 OUTLOOK

Spanning the centuries between 33 B.C. (Vitruvius, 1999) and the Italian renaissance (Vignola-Barozzi 1582), essential works have outlined and shaped the rhetorical architectural theory in Western cultures. Therefore, in order to prevent confounding variables, all subjects who participated in this study were born and raised in Western cultures. However, it would be interesting to see whether our result of increased familiarity effects for high- compared to low-ranking buildings (i.e. decreased N400 potentials and increased dm effects) would apply also to subjects who were raised in different non-Western environments and, thus, have been familiarised to other architectural modules and ornamental styles that do not follow the classical decorum theory. Indeed, preliminary results from a study that is being conducted at the moment in Bejing investigating visual processing with our stimuli set in Asian students shows no differentiation between high- and low-ranking buildings in the N400 time window, thus confirming culture specific impacts of the architectural decorum on the perception of high- and low-ranking stimuli (Mecklinger et al., in preparation). Furthermore, future work may investigate whether the present findings of differentiating ERP responses relative to different decorum stimuli would also apply to other types of stimulus material, e.g. high- and low-ranking verbal stimuli. In this respect, we aim to build up a cooperation with the University of Saarbrücken (Prof. Axel Mecklinger) to explore in greater detail the concept of architectural decorum.

Our results suggest that the hippocampus proper does indeed contribute critically to architectural ranking inference and that this process is compromised in medial temporal lobe epilepsy with hippocampal sclerosis. However, our findings cannot adjudicate the question of whether hippocampal contributions to the visual processing of buildings are more related to episodic memory processes or the semantic processing of visual stimuli. High-ranking buildings could elicit prototypical (or for that matter "false") memories by alluring recollections of sublime buildings from episodic memory and/or they could be easier to verbalize. Future studies may want to address this question.

Prof. Manila Vannucci from the University of Florence is currently exploring in more detail the aspect of prototypicality of our stimulus material. Adopting the same set of pictures applied in our studies, she aims to probe the processing of familiarity and visual complexity of high- and low-ranking buildings. In addition, comparing experts in architecture with laymen, she recently conducted an experiment on the aesthetic judgment of the two kinds of building categories and their phase-randomized transformed version. Preliminary data are promising and being further analyzed.

To conclude, by combining theory of architecture and design with a neuroscientific method the present work has revealed initial results that we hope will give rise to continuing studies that may further investigate the underlying mechanisms of the perception of high- and low-ranking stimuli based on the architectural decorum.

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9 PUBLICATIONS

9.1 Papers

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9.2 Posters

Vannucci M, **Oppenheim I**, Mühlmann H, Gabriel R, Krämer G, Grunwald T. *Human brain sensitivity to architectural ranking: The contribution of the hippocampus.* International Association of Empirical Aesthetics IAEA, XI Biennal Meeting, Dresden 25-28 August 2010.

Oppenheim I, Jokeit H, Gabriel R, Mühlmann H, Blechinger G, Krämer G, Grunwald T. *Memory Processes Associated with the Perception of High-Ranking Buildings.* ZNZ Symposium, Zurich, Sep 12, 2008.

Oppenheim I, Mothersill IW, Hilfiker P, Jokeit H, Kurthen M, Mühlmann H, Blechinger G, Grunwald T. *Buildings and Brains: Processing of Architectural Stimuli in a Visual Object Decision Task.* ZNZ Symposium, Zurich, Sep 14, 2007.

Oppenheim I, Grunwald T. *New Sounds, Old Pictures: Why the Hippocampus Attends to Language.* Gemeinsame Jahrestagung der Deutschen, Österreichischen und Schweizerischen Sektionen der Internationalen Liga gegen Epilepsie ILAE. Basel, May 16 – 19, 2007.

9.3 Talks

Buildings and Brains: Processing of Architectural Stimuli. OBOB Symposium, University of Konstanz, Jul 7, 2009.

Buildings and Brains: Processing of Architectural Stimuli in a Visual Object Decision Task. ZNZ Symposium, Data Blitz. Zurich, Sep 14, 2007.

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